



BLA 125141/S-223
BLA 125291/S-151

SUPPLEMENT APPROVAL

Genzyme Corporation
Attention: Christina Fang, PharmD
Global Regulatory Affairs Team Lead- Rare Diseases
50 Binney Street
Cambridge, MA 02142

Dear Dr. Fang:

Please refer to your supplemental biologics license application (sBLA), dated October 29, 2019, submitted under section 351(a) of the Public Health Service Act for Myozyme (alglucosidase alfa) injection (BLA 125141) and Lumizyme (alglucosidase alfa) for injection (BLA 125291).

This Prior Approval supplemental biologics application provides for updates to the Prescribing Information in Warnings and Precautions and Adverse Reactions, Immunogenicity based on the results of Myozyme PMC 2497-6 study.

APPROVAL & LABELING

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, via the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 601.14(b)] in structured product labeling (SPL) format, as described at FDA.gov,¹ that is identical to the enclosed labeling (Prescribing Information) and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements.

Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*.²

¹ <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

² We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

The SPL will be accessible via publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this BLA, including pending "Changes Being Effected" (CBE) supplements, for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 601.12(f)] in Microsoft Word format that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

FULFILLMENT OF POSTMARKETING REQUIREMENT(S)/COMMITMENT(S)

We have received your submission dated Oct 29, 2019, containing the final report for the following postmarketing commitment listed in the April 28, 2006, approval letter for Myozyme BLA 125141:

PMC (b) (4) **6:** Genzyme commits to designing and implementing an immune tolerance protocol in Pompe disease patients who have significant antibody titers, or the presence of neutralizing antibody, and are failing treatment. Genzyme commits to designing and implementing a preventive immune tolerance protocol in Pompe disease patients at high risk for the development of significant immune responses to the product. This would involve 1) establishing the correlation among genotype, the level of glucosidase protein (non-enzymatic assay), and the presence and levels of binding, IgE, and neutralizing antibodies over time, using validated assays; and 2) developing an immune tolerance regimen that would be implemented before or concomitant with onset of therapy for those at high risk. Additionally, Genzyme commits to monitoring antibody positive patients, whose immune responses are not associated with loss of efficacy or severe hypersensitivity responses, at regular intervals over an extended period of time (i.e., 18-24 months) to specifically assess if a sub-population of patients become tolerant with routine treatment. Reports from preclinical studies to assess potential tolerance regimens and a commitment for timelines for a subsequent clinical study will be submitted to CDER by December 29, 2006. Genzyme commits to developing a protocol that will be used to provide guidance to physicians for the use of tolerance-inducing regimens for patients who are currently failing treatment because of a robust antibody response and to submit this protocol by October 31, 2006.

We have reviewed your submission and conclude that the above commitment is fulfilled.

We remind you that there are postmarketing commitments listed in the April 28, 2006, approval letter that are still open.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the Prescribing Information to:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705-1266

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format—Promotional Labeling and Advertising Materials for Human Prescription Drugs*.³

As required under 21 CFR 601.12(f)(4), you must submit final promotional materials, and the Prescribing Information, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at FDA.gov.⁴ Information and Instructions for completing the form can be found at FDA.gov.⁵ For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see FDA.gov.⁶

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved BLA (in 21 CFR 600.80 and in 21 CFR 600.81).

If you have any questions, call Jenny Doan, Regulatory Project Manager, at (301) 796-1023..

Sincerely,

{See appended electronic signature page}

³ When final, this guidance will represent the FDA's current thinking on this topic. For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

⁴ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>

⁵ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>

⁶ <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>

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Joyce Korvick, M.D., M.P.H.
Deputy Director for Safety
Division of Gastroenterology and Inborn Errors
Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

ENCLOSURE:

- Prescribing Information- Myozyme
- Prescribing Information- Lumizyme

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

JOYCE A KORVICK
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