



BLA 103979/S-5312

**SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING
COMMITMENT**

Genzyme Corporation
Attention: Catherine Viel
Regulatory Strategist, Global Regulatory Affairs
49 New York Avenue
Framingham, MA 01701

Dear Catherine Viel:

Please refer to your supplemental biologics license application (sBLA), dated and received August 7, 2023, and your amendments, submitted under section 351(a) of the Public Health Service Act for Fabrazyme (agalsidase beta) for injection.

This Prior Approval supplemental biologics application provides for changes to the labeling which include:

- Additions to the Prescribing Information (PI), section 5.1 Hypersensitivity Reactions Including Anaphylaxis, pertaining to considerations to address possible hypersensitivity reactions prior to treatment with Fabrazyme.
- Changes to the PI, Section 8 Use In Specific Populations, based on information collected to fulfill postmarketing commitment (PMC) 2465-3.
- Additional updates and reorganization throughout the PI to align with current regulations, labeling practices, and guidance documents.

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 (text for the Prescribing Information) and include the labeling changes proposed in any pending “Changes Being Effectuated” (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

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 Effectuated” (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).

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because none of these criteria apply to your application, you are exempt from this requirement.

FULFILLMENT OF POSTMARKETING COMMITMENT

We have reviewed your submission dated August 7, 2023, and your amendments dated November 30, 2023, and January 10, 2024, comprising the final report for the following postmarketing commitment listed in the April 24, 2003, approval letter for BLA 103979.

2465-3 Genzyme commits to continuing the registry of patients with Fabry disease being treated with Agalsidase beta that was established to obtain long-term clinical status information. This study will be revised so that detailed clinical status information is collected at study entry and on a 6 to 12-

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>.

month basis for at least 15 years. Genzyme commits to conducting a sub-study within the registry that will evaluate the effect of Agalsidase beta on pregnancy and lactation. The registry data will be analyzed at yearly intervals and the results will be submitted in your annual reports for BB-IND 7616. Information will also be collected on clinical status, adverse events, assessment of immunogenicity and potential effects of antibody formation. This study was initiated in Europe on January 30, 2001. An amended study protocol will be submitted to CBER by September 30, 2003, and this revised study will be initiated by January 31, 2004. The final study report under this registry will be submitted to CBER by September 30, 2020.

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

This completes all of your postmarketing requirements and postmarketing commitments acknowledged in our April 24, 2003, letter. You are not required to report on the status of closed (released or fulfilled) PMRs/PMCs in your annual report required under 21 CFR 601.70 of the FD&CA.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see the final 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

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).

³ For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/media/128163/download>.

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

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

If you have any questions, contact Diego Diaz, Regulatory Project Manager, via email at Diego.Diaz@fda.hhs.gov or at (301) 796-7182.

Sincerely,

{See appended electronic signature page}

Catherine Pilgrim-Grayson, MD, MPH
Director (Acting)
Division of Rare Diseases and Medical Genetics
Office of Rare Diseases, Pediatrics, Urology and
Reproductive Medicine
Center for Drug Evaluation and Research

ENCLOSURE:

- Content of Labeling
 - Prescribing Information

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/

CATHERINE A PILGRIM-GRAYSON
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