BLA 103979/S-5309

SUPPLEMENT APPROVAL

Genzyme Corporation
Attention: Hiren Patel
Sr Manager, US, Global Regulatory Affairs
50 Binney Street
Cambridge, MA 02142

Dear Mr. Patel:

Please refer to your supplemental biologics license application (sBLA), dated and received February 14, 2020, and your amendments, submitted under section 351(a) of the Public Health Service Act for Fabrazyme (agalsidase beta).

We acknowledge receipt of your major amendment dated November 24, 2020, which extended the goal date by three months.

This Prior Approval supplemental biologics application provides for the traditional approval of Fabrazyme for the treatment of adult and pediatric patients 2 years of age and older with confirmed Fabry disease.

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 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).

SUBPART E FULFILLED

We approved this BLA under the regulations at 21 CFR 601 Subpart E for Accelerated Approval of Biological Products for Serious or Life-Threatening Illnesses. Approval of this supplement fulfills your commitments made under 21 CFR 601.41.

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 this drug product for this indication has an orphan drug designation, you are exempt from this requirement.

FULFILLMENT OF POSTMARKETING REQUIREMENT

This supplemental application contained the final report for the following postmarketing requirement listed in the May 13, 2008, complete response/postapproval postmarketing requirement letter.

2421-2 Genzyme commits to performing additional analyses of the data obtained in the registry of patients with Fabry disease being treated with Agalsidase beta that was established to obtain long-term clinical status information. Additional analyses of the registry data are to be performed for the purpose of establishing the clinical benefit of Fabrazyme on progression of renal disease and other end-organ disease endpoints in patients with Fabry disease. Additional analyses to be performed include the following:

a) Progression of renal disease, including assessment of time of onset of proteinuria, hypertension, chronic renal insufficiency, end-stage renal disease, and death.
b) Exploration of the effects of endogenous αGAL activity and genetic mutations on progression of renal disease, the occurrence of significant clinical events, and the development of anti-recombinant-human-αGAL (anti-r-hαGAL) IgG antibodies.
c) Progression of renal disease by age of initiation of ERT with Fabrazyme for age groups such as <10 years of age, ≥10 to <15 years of age, ≥15 to 20 years of age, and in 10 year increments at >20 years of age.
d) Progression of renal disease by treatment administered, including ERT with Fabrazyme or no treatment. Reports will include data on patients who have received other Fabry specific treatments
e) Progression of renal disease by GFR status (≥60 ml/min/1.73 m^2 or <60 ml/min/1.73 m^2) at initiation of ERT with Fabrazyme.
f) Time of first significant clinical event.
g) Analysis of anti-r-hαGAL IgG antibodies titers on the progression of renal disease and the occurrence of significant clinical events.

A final analysis plan for the registry study protocol will be submitted to CDER by October 25, 2008. The final study report under this registry will be submitted to CDER by July 30, 2021.

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

We remind you that there is a postmarketing commitment listed in the April 24, 2003, approval letter that is still open.

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,

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

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]

All promotional materials for your drug product that include representations about your drug product must be promptly revised to make it consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 601.12(a)(4)]. The revisions to your promotional materials should include prominent disclosure of the important new safety information that appears in the revised labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 601.12(a)(4).

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 Michael G. White, PhD, Chief, Project Management Staff, at 240-402-6149.

Sincerely,

{See appended electronic signature page}

Patroula Smpokou, M.D.
Deputy Director
Division of Rare Diseases and Medical Genetics (DRDMG)
Office of Rare Diseases, Pediatrics, Urologic and Reproductive Medicine (ORPURM)
Center for Drug Evaluation and Research

ENCLOSURE:

- Content of Labeling
    - Prescribing Information

[4] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

---

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/

PATROULA I SMPOKOU
03/11/2021 11:17:53 AM