U.S. FOOD & DRUG ADMINISTRATION

BLA 125513/S-033

SUPPLEMENT APPROVAL

Alexion Pharmaceuticals, Inc.
Attention: Mary Lyons
Director, Global Labeling Operations
100 College Street
New Haven, CT 06510

Dear Mary Lyons:

Please refer to your supplemental biologics license application (sBLA), dated and received April 26, 2024, submitted under section 351(a) of the Public Health Service Act for Strensiq (asfotase alfa) injection.

We also refer to our letter dated March 8, 2024, and our corrected Safety Labeling Change Notification letter dated March 28, 2024, notifying you, under Section 505(o)(4) of the FDCA, of new safety information that we determined should be included in the labeling for enzyme replacement therapies (ERTs) to treat inborn errors of metabolism. ERTs represent a class of products that have a serious risk of hypersensitivity reactions, including anaphylaxis.

This supplemental biologics license application provides for revisions to the labeling for Strensiq. The agreed upon changes to the language included in our March 28, 2024, Safety Labeling Change Notification letter are as follows (additions are noted by underline and deletion are noted by ~~strikethrough~~).

> Patients treated with enzyme replacement therapies have experienced life-threatening hypersensitivity reactions, including anaphylaxis. Anaphylaxis has occurred during the early course of enzyme replacement therapy and after extended duration of therapy~~.~~ (b) (4) Initiate STRENSIQ under the supervision of a healthcare provider with appropriate medical monitoring and support measures. If a severe hypersensitivity reaction (e.g., anaphylaxis) occurs, discontinue STRENSIQ and immediately initiate appropriate medical treatment, including use of epinephrine. Inform patients of the symptoms of life-threatening hypersensitivity reactions, including anaphylaxis and to seek immediate medical care should symptoms occur. *[see Warnings and Precautions* (b) (4) (5.1)].

APPROVAL & LABELING

We have completed our review of this application. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling with a minor editorial revision listed below and reflected in the enclosed Patient Packet Insert labeling.

In the Patient Information sheet, under the section "What are the possible side effects of SRENSIQ?", following the colon at the end of the phrase "STRENSIQ may cause serious side effects, including:", a carriage return and bullet point were inserted preceding "severe allergic (hypersensitivity) reactions" as depicted below:

What are the possible side effects of STRENSIQ?

STRENSIQ may cause serious side effects, including:

- **severe allergic (hypersensitivity) reactions. See "What is the most important information I should know about STRENSIQ?"**

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 Patient Package Insert) 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]

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).

[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.

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.

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]

You must submit final promotional materials and Prescribing Information, accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. 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 that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety- related information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety-related 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 314.70(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).

[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, CDR Cheronda 'Roni' Cherry-France, Safety Regulatory Project Manager at cheronda.cherry-france@fda.hhs.gov or (301) 796-7295.

Sincerely,

{See appended electronic signature page}

Yuliya Yasinskaya, MD
Deputy Director
Division of Rare Diseases and Medical Genetics
Office of Rare Diseases, Pediatrics, Urologic and Reproductive Medicine
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Patient Package Insert
  - Instructions for Use (previously approved June 12, 2020)

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/

YULIYA I YASINSKAYA
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