BLA 761112/S-007

SUPPLEMENT APPROVAL

Ablynx NV
Attention: Valeria Winslow, PhD
Global Regulatory Affairs
225 Second Avenue
Waltham, MA 02451

Dear Dr. Winslow:

Please refer to your supplemental biologics license application (sBLA), dated and received September 18, 2020, submitted under section 351(a) of the Public Health Service Act for Cablivi (caplacizumab-yhdp) for injection.

This "Changes Being Effected" supplemental biologics application provides for modifications to Section 6 of the United States Prescribing Information (USPI) – Adverse Drug Reaction to include "injection site erythema" under Section 6.3 – Postmarketing Experience.

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.

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).

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

POSTMARKETING COMMITMENTS NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

PMC 3568-2 To conduct a study to demonstrate that the pre-filled syringe plunger movement during air transport does not impact product sterility.

The timetable you submitted on January 8, 2019, states that you will conduct this study according to the following schedule:

Final Report Submission: 08/19

PMC 3568-3 To repeat the (b) (4) bacterial retention study using a non-bactericidal surrogate solution with physical attributes comparable to the product.

The timetable you submitted on September 25, 2019, states that you will conduct this study according to the following schedule:

Final Report Submission: 12/19

PMC 3568-4 To validate shipping of bulk drug substance (b) (4) during summer conditions.

The timetable you submitted on January 8, 2019, states that you will conduct this study according to the following schedule:

Final Report Submission: 03/19

PMC 3568-5 To perform the testing for resistance to overriding for sWFI syringe in accordance to ISO-80369-7.

The timetable you submitted on January 8, 2019, states that you will conduct this study according to the following schedule:

Final Report Submission: 08/19

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 athttps://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 Brittany Garr-Colón, MPH, Regulatory Project Manager, at (301) 796-6153 or Brittany.Garr-Colon@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Ann Farrell, MD
Director
Division of Nonmalignant Hematology
Office of Cardiology, Hematology,
Endocrinology, and Nephrology
Center for Drug Evaluation and Research

ENCLOSURE(S):

- 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/

ANN T FARRELL
12/16/2020 06:10:33 PM