



Our STN: BL 125644/0

BLA APPROVAL
June 19, 2018

Bio Products Laboratory
Attention: Mary Ann Lamb, PhD
Bio Products Laboratory USA Inc.
Suite C-190
302 East Pettigrew Street
Durham, NC 27701

Dear Dr. Lamb:

Please refer to your Biologics License Application (BLA) for albumin, human -kjda 5% and 25%, dated December 15, 2017, received December 15, 2017, submitted under section 351(a) of the Public Health Service Act (PHS Act).

We have approved your BLA for albumin, human-kjda 5% and albumin, human-kjda 25% effective this date. You are hereby authorized to introduce or deliver albumin, human-kjda 5% and albumin, human-kjda 25% for introduction into interstate commerce, under your existing Department of Health and Human Services U.S. License No. 1811. Albumin, human-kjda 5% and albumin, human-kjda 25% are indicated for hypovolemia, ascites, hypoalbuminemia including from burns, acute nephrosis, acute respiratory distress syndrome and cardipulmonary bypass.

Under this license, you are approved to manufacture albumin, human-kjda 5% and albumin, human-kjda 25% at your facility located at Elstree, United Kingdom. The final formulated product will be manufactured, filled, labeled and packaged at the Bio Products Laboratory, Dagger Lane Elstree Hertfordshire WD63BX, United Kingdom.

You may label your product with the proprietary name ALBUMINEX and market the 5% solution in 250 mL and 500 mL glass vials; the 25% solution in 50 mL and 100 mL glass vials.

We did not refer your application to the Blood Products Advisory Committee because our review of information submitted in your BLA, did not raise concerns or controversial issues that would have benefited from an advisory committee discussion.

DATING PERIOD

The dating period for ALBUMINEX (albumin, human - kjda) 5% and 25% shall be 36 months from the date of manufacture when stored at no higher than 30 °C. The date of manufacture shall be defined as the date of final sterile filtration of the formulated drug product OR as otherwise appropriate.

FDA LOT RELEASE

Please submit final container samples of the product in final containers together with protocols showing results of all applicable tests. Please submit protocols showing results of all applicable tests. You may not distribute any lots of product until you receive a notification of release from the Director, Center for Biologics Evaluation and Research (CBER).

BIOLOGICAL PRODUCT DEVIATIONS

You must submit reports of biological product deviations under 21 CFR 600.14. You should identify and investigate all manufacturing deviations promptly, including those associated with processing, testing, packaging, labeling, storage, holding and distribution. If the deviation involves a distributed product, that may affect the safety, purity, or potency of the product, and meets the other criteria in the regulation, you must submit a report on Form FDA 3486 to the Director, Office of Compliance and Biologics Quality, at the following address:

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center
10903 New Hampshire Ave.
WO71-G112
Silver Spring, MD 20993-0002

MANUFACTURING CHANGES

You must submit information to your BLA for our review and written approval under 21 CFR 601.12 for any changes in, including but not limited to, the manufacturing, testing, packaging or labeling of albumin, human-kjda 5% and albumin, human -kjda 25%, or in the manufacturing facilities.

LABELING

Under 21 CFR 201.57(c)(18), patient labeling must be referenced in section 17 PATIENT COUNSELING INFORMATION. Patient labeling must be available and may either be reprinted immediately following the full prescribing information of the package insert or accompany the prescription product labeling.

We hereby approve the draft package insert labeling, and the draft carton and container labeling submitted under amendment #41, dated June 12, 2018.

Please provide your final content of labeling including the carton and container labels in Structured Product Labeling (SPL) format. All final labeling should be submitted as Product Correspondence to this BLA 125644 at the time of use (prior to marketing) and include implementation information on Form FDA 356h.

In addition, please submit the final content of labeling (21 CFR 601.14) in SPL format via the FDA automated drug registration and listing system, (eLIST) as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. 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* at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>.

You may submit two draft copies of the proposed introductory advertising and promotional labeling with Form FDA 2253 to the Advertising and Promotional Labeling Branch at the following address:

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center
10903 New Hampshire Ave.
WO71-G112
Silver Spring, MD 20993-0002

You must submit copies of your final advertising and promotional labeling at the time of initial dissemination or publication, accompanied by Form FDA 2253 (21 CFR 601.12(f)(4)).

All promotional claims must be consistent with and not contrary to approved labeling. You should not make a comparative promotional claim or claim of superiority over other products unless you have substantial evidence or substantial clinical experience to support such claims (21 CFR 202.1(e)(6)).

ADVERSE EVENT REPORTING

You must submit adverse experience reports in accordance with the adverse experience reporting requirements for licensed biological products (21 CFR 600.80) and you must submit distribution reports as described in 21 CFR 600.81. For information on adverse experience reporting, please refer to the guidance for industry *Providing Submissions in Electronic Format – Postmarketing Safety Reports* at <http://www.fda.gov/Drugs/DrugSafety/ucm400526.htm> and FDA's Adverse Event reporting System website <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/ucm115894.htm>. For information on distribution reporting, please refer to the guidance for industry *Electronic Submission of Lot Distribution Reports* at <http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Post-MarketActivities/LotReleases/ucm061966.htm>.

In addition, you must submit adverse event reports for any infectious disease transmission within 15 days after learning of the event. Infectious disease transmission refers to an adverse event that involves suspected or confirmed transmission of an infectious agent, whether the recipient develops the infectious disease or only has serologic or other evidence. If an infectious disease transmission event is serious and

unexpected, you must submit a 15-day “alert report,” as required under 21 CFR 600.80 (c)(1)(i). Infectious disease transmission events that do not meet criteria for expedited submission require periodic reports and must be submitted as individual safety case reports within 15 days, as authorized under 21 CFR 600.80(c)(2)(i). You should submit reports for all other non-expedited adverse events under the periodic reporting requirements specified in 21 CFR 600.80(c)(2).

PEDIATRIC REQUIREMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, 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 in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for this application because necessary studies are impossible or highly impractical due to the small numbers and geographic dispersion of pediatric patients utilizing albumin products.

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

We acknowledge your written commitments as described in your letters of April 20, 2018, and April 27, 2018, as outlined below:

1. Bio Products Laboratory commits to provide study results for leachables evaluated at the final shelf life for drug product albumin, human -kjda 5% and 25% as a post marketing commitment, submitting study results within (b) (4) of approval.

Final protocol submission: (b) (4)

2. Bio Products Laboratory commits to perform method validation for the determination of (b) (4) using well characterized standards to establish valid range, repeatability, linearity and precision. In-process samples from (b) (4) and final product samples should be tested against the result obtained using the established standards. Bio Products Laboratory . will submit the results from the validation within (b) (4) of approval.

Final Report Submission: (b) (4)

We request that you submit information concerning nonclinical and chemistry, manufacturing, and control postmarketing commitments and final reports to your BLA 125644. Please refer to the sequential number for each commitment.

Please use the following designators to prominently label all submissions, including supplements, relating to these postmarketing study commitments as appropriate:

- **Postmarketing Commitment – Status Update**
- **Postmarketing Commitment – Final Study Report**
- **Supplement contains Postmarketing Commitment – Final Study Report**

For each postmarketing commitment not subject to the reporting requirements of 21 CFR 601.70, you may report the status to FDA as a **Postmarketing Commitment – Status Update**. The status report for each commitment should include:

- the sequential number for each study as shown in this letter;
- the submission number associated with this letter;
- describe what has been accomplished to fulfill the non-section 506B PMC; and,
- summarize any data collected or issues with fulfilling the non-section 506B PMC.

When you have fulfilled your commitment, submit your final report as **Postmarketing Commitment – Final Study Report** or **Supplement contains Postmarketing Commitment – Final Study Report**.

POST APPROVAL FEEDBACK MEETING

New biological products qualify for a post approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, please contact the Regulatory Project Manager for this application.

Sincerely,

Nicole Verdun, MD
Acting Office Director
Office of Blood Research and Review
Center for Biologics Evaluation and Research