DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 200656

**NDA APPROVAL**

Fresenius Kabi USA, LLC
Attention: Lakshmi Rebbapragada
Sr. Regulatory Specialist
Three Corporate Drive
Lake Zurich, IL 60047

Dear Ms. Rebbapragada:

Please refer to your New Drug Application (NDA) dated January 28, 2011, received January 28, 2011, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Kabiven and Perikabiven (amino acids, electrolytes, dextrose and lipid injectable emulsion).

We acknowledge receipt of your amendments dated March 10, 2011, April 6, 2011, April 25, 2011, May 10, 2011, June 17, 2011, July 7, 2011, July 27, 2011, August 5, 2011, August 19, 2011, September 2, 2011, September 7, 2011, September 16, 2011, October 13, 2011, October 21, 2011, November 11, 2011, November 18, 2011, June 1, 2012, August 24, 2012, November 2, 2012, November 16, 2012, May 6, 2013, August 7, 2013, August 26, 2013, November 1, 2013, November 22, 2013, January 13, 2014, January 15, 2014, January 31, 2014, February 20, 2014, March 25, 2014, April 29, 2014, May 13, 2014, May 27, 2014, May 30, 2014, June 2, 2014, June 6, 2014, August 7, 2014, August 11, 2014, August 18, 2014, August 19, 2014, August 21, 2014, August 22, 2014, and August 25, 2014.

The November 22, 2013, submission constituted a complete response to our November 21, 2011, action letter.

This new drug application provides for the use of Kabiven and Perikabiven (amino acids, electrolytes, dextrose and lipid injectable emulsion) as a source of calories, protein, electrolytes and essential fatty acids for adult patients requiring parenteral nutrition when oral or enteral nutrition is not possible, insufficient, or contraindicated.

We have completed our review of this application. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text and with the minor editorial revisions indicated in the enclosed labeling.

## CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (text for the package insert). 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*, available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

## CARTON AND IMMEDIATE CONTAINER LABELS

We acknowledge your August 21, 2014, submission containing final printed carton and container labels.

## MARKET PACKAGE

Please submit one market package of the drug product when it is available to the following address:

CDR Matthew Brancazio, Pharm.D.
Food and Drug Administration
Center for Drug Evaluation and Research
White Oak Building 22, Room: 5345
10903 New Hampshire Avenue
Silver Spring, Maryland
*Use zip code* **20903** *if shipping via United States Postal Service (USPS).*
*Use zip code* **20993** *if sending via any carrier other than USPS (e.g., UPS, DHL, FedEx).*

## REQUIRED PEDIATRIC ASSESSMENTS

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(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for ages 0 to 2 years because the product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in this age group **and** is not likely to be used in a substantial number of pediatric patients in this group. Pediatric patients less than 2 years of age generally require specific, individually prepared parenteral nutrition. Based on the nutritional requirement calculations, Kabiven and Perikabiven (amino acids, electrolytes, dextrose and lipid injectable emulsion) may not provide adequate nutrition for patients less than 2 years of age.

We are deferring submission of your pediatric study for ages 2 to 16 years for this application because this product is ready for approval for use in adults and the pediatric study has not been completed.

Your deferred pediatric study required by section 505B(a) of the FDCA is a required postmarketing study. The status of this postmarketing study must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(B) of the FDCA. The required study is listed below.

2772-1 Prospective, randomized (1:1), open-label, parallel group, active controlled, multicenter study to assess safe and effective doses of Kabiven (amino acids, electrolytes, dextrose and lipid injectable emulsion) in pediatric patients aged 2 to 16 years.

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| Final Protocol Submission: | 02/2015 |
| Study Completion: | 08/2017 |
| Final Report Submission: | 08/2018 |

Submit the protocol to your IND 105282 with a cross-reference letter to this NDA.

Reports of this required pediatric postmarketing study must be submitted as a new drug application (NDA) or as a supplement to your approved NDA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

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

We remind you of your postmarketing commitments:

2772-2 Conduct testing for (b) (4) content in the Kabiven or Perikabiven product. The testing will be divided into two phases:

1. Test batches of freshly manufactured product using six different batches of the (b) (4) bag.
2. Test six different batches of product at expiry.

The timetable you submitted on August 25, 2014, states that you will conduct this study according to the following schedule:

Final Report Phase 1: 03/16
Final Report Phase 2: 12/18

Submit clinical protocols to your IND 105282 for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii) you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled "**Postmarketing Commitment Protocol**," "**Postmarketing Commitment Final Report**," or "**Postmarketing Commitment Correspondence**."

## PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf. Information and Instructions for completing the form can be found at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

## REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call CDR Matthew Brancazio, Pharm.D., Regulatory Project Manager, at (301) 796-5343.

Sincerely,

*{See appended electronic signature page}*

Joyce Korvick, M.D., M.P.H.
Deputy Director for Safety
Division of Gastroenterology and Inborn Errors Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosure(s):
Content of Labeling
Carton and Container Labeling

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**

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/s/

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JOYCE A KORVICK
08/25/2014