NDA 17643/S-083
NDA 18449/S-050, S-051
NDA 19942/S-021
NDA 20248/S-027, S-028

SUPPLEMENT APPROVAL

Fresenius Kabi USA, LLC
Attention: Peter Baer
Senior Regulatory Specialist
Three Corporate Drive
Lake Zurich, IL 60047

Dear Mr. Baer,

Please refer to your supplemental new drug applications (sNDAs) dated and received on October 13, 2022, and February 21, 2023, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) the following:

Application	Supplement	Drug Product
NDA 017643	S-083	Intralipid 10% (lipid injectable emulsion), for intravenous use
NDA 018449	S-050 S-051	Intralipid 20% (lipid injectable emulsion), for intravenous use
NDA 019942	S-021	Intralipid 30% (lipid injectable emulsion), for intravenous use (Pharmacy Bulk Package)
NDA 020248	S-027 S-028	Intralipid 20% (lipid injectable emulsion), for intravenous use (Pharmacy Bulk Package)

These supplemental applications, sNDA 18449/S-050 and sNDA 20248/S-027, provide for the conversion of the Prescribing Information into Physician Labeling Rule (PLR) format and a voluntary compliance with the Pregnancy and Lactation Labeling Rule (PLLR) content and format requirements.

We also refer to our letter dated January 24, 2023, notifying you, under Section 505(o)(4) of the FDCA, of new safety information that we have determined should be included in the labeling for intravenous lipid emulsions (ILEs), including Intralipid. This information pertains to the risk of clinical decompensation after rapid infusion of ILEs.

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 the minor editorial revisions listed below and reflected in the enclosed labeling.

- sNDA 18449/S-050 and sNDA 20248/S-027

  - In the **HIGHLIGHTS OF PRESCRIBING INFORMATION**,

    - In **RECENT MAJOR CHANGES** section, added the following:
      - Contraindications (4) 5/2023

    - In **WARNINGS AND PRECAUTIONS**, Risk of Parenteral Nutrition-Associated Liver Disease (PNALD), added a reference to subsection 6.1

  - In the **FULL PRESCRIBING INFORMATION**, section 5.2 **Parenteral Nutrition-Associated Liver Disease and Other Hepatobiliary Disorders,** corrected the references relating to *[see Adverse Reactions (6.1), Use in Specific Populations (8.4)]*

- sNDA 017643/S-083 and sNDA 019942/ S-021

  - Edited revision date to the action month of May

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 FDA.gov.[1] Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information), with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

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 from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in Microsoft Word

[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.

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).

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).

PATENT LISTING REQUIREMENTS

Pursuant to 21 CFR 314.53(d)(2) and 314.70(f), certain changes to an approved NDA submitted in a supplement require you to submit patent information for listing in the Orange Book upon approval of the supplement. You must submit the patent information required by 21 CFR 314.53(d)(2)(i)(A) through (C) and 314.53(d)(2)(ii)(A) and (C), as applicable, to FDA on Form FDA 3542 within 30 days after the date of approval of the supplement for the patent information to be timely filed (see 21 CFR 314.53(c)(2)(ii)). You also must ensure that any changes to your approved NDA that require the submission of a request to remove patent information from the Orange Book are submitted to FDA at the time of approval of the supplement pursuant to 21 CFR 314.53(d)(2)(ii)(B) and 314.53(f)(2)(iv).

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[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

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 Thao Vu, Safety Regulatory Project Manager, at (240) 402-2690.

Sincerely,

{See appended electronic signature page}

Judith A. Racoosin, M.D., M.P.H.
Deputy Director for Safety
Division of Hepatology and Nutrition
Office of Immunology and Inflammation
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURE:

- 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/

JUDITH A RACOOSIN
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