NDA 204508/S-019
NDA 204508/S-021

SUPPLEMENT APPROVAL

Baxter Healthcare Corporation
Attention: Nicole Rodgers
Senior Manager, Global Regulatory Affairs
25212 W. Illinois, Route 120
Round Lake, IL 60073

Dear Ms. Rodgers,

Please refer to your supplemental new drug application (sNDA) dated and received on March 18, 2022, and February 10, 2023, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Clinolipid (lipid injectable emulsion), for intravenous use.

The "Changes Being Effected" sNDA, S-019, proposes to update the following:

- The strengths presentation as the total quantity of lipid (g) per total volume (mL) for the 250ml and 500ml carton and container labels, for Section 3, Dosage Forms and Strengths, and Section 16, How Supplied/Storage and Handling of the prescribing information (PI).

- Additionally, the Warnings and Precautions section of labeling for the plant-based intravenous lipid emulsions, including Clinolipid, are being updated:

    - Section 5, WARNINGS and PRECAUTIONS

        - Add Section 5.1 Parenteral Nutrition-Associated Liver Disease and Other Hepatobiliary Disorders based

        - Updated the other subsections to reflect class labeling changes intended to improve clarity

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 Clinolipid. This information pertains to the risk of clinical decompensation after rapid infusion of ILEs.

APPROVAL & LABELING

We have completed our review of this application, as amended. 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.

- In the **HIGHLIGHTS OF PRESCRIBING INFORMATION,**
  - In **RECENT MAJOR CHANGES** (RMC) section, added the following:
    - Warnings and Precautions (5.1, 5.2)

- In the **FULL PRESCRIBING INFORMATION**, section 5.2 **Parenteral Nutrition-Associated Liver Disease and Other Hepatobiliary Disorders,** added the vertical line on the left edge corresponding to the new RMC listed in Highlights of Prescribing Information

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 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.

CARTON AND CONTAINER LABELING

Submit final printed carton and container labeling that are identical to the enclosed carton and container labeling as soon as they are available, but no more than 30 days after they are printed. Please submit these labeling electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*. For administrative purposes, designate this submission "**Final Printed Carton and Container Labeling for approved NDA 204508/S-021**." Approval of this submission by FDA is not required before the labeling is used.

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 information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety 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 NDA (21 CFR 314.80 and 314.81).

[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, call Thao Vu, Safety Regulatory Health 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

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
- Carton and Container Labeling

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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