

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER: 21-135

APPROVAL LETTER



Food and Drug Administration
Rockville MD 20857

NDA 21-135

Luitpold Pharmaceuticals, Inc.
c/o Arent Fox Kintner Plotkin & Kahn, PLLC
Attention: Peter S. Reichertz, Esq.
1050 Connecticut Avenue
Washington, D.C. 20036-6378

Dear Mr. Reichertz:

Please refer to your new drug application (NDA) dated August 6, 2000, received August 6, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Venofer® (iron sucrose injection).

We acknowledge receipt of your submissions dated September 22, October 6, October 15, October 19, October 22, October 27, November 16, November 22, December 7, 1999 and January 14, February 22, April 19, May 3, May 31, June 6, June 13, June 16, June 20, June 30, August 10, September 28, October 12, October 26, October 31, November 1, and November 6, 2000.

This new drug application provides for the use of Venofer® (iron sucrose injection) for the treatment of iron deficiency anemia in patients undergoing chronic hemodialysis who are receiving supplemental erythropoietin therapy.

We have completed the review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon enclosed labeling text. Accordingly, the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert) and submitted draft labeling (immediate container and carton labels submitted August 6, 2000) incorporating the following revisions to the vial and carton labels: (1) change the phrase, "IRON (III) HYDROXIDE SUCROSE COMPLEX" to "IRON SUCROSE IN WATER FOR INJECTION" and (2) add a space for the lot number and expiration date. Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. Alternatively, you may submit the FPL electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDAs* (January 1999). For administrative purposes, this submission

should be designated "FPL for approved NDA 21-135." Approval of this submission by FDA is not required before the labeling is used.

We remind you of your post marketing commitments specified in your submission dated November 6, 2000. These commitments, along with any completion dates agreed upon, are listed below.

1. examine the worldwide safety database for Venofer® for occurrence of adverse events in pediatric patients by age group (neonates, infants, children, adolescents). Attempt to obtain further information on the 5 reported cases of necrotizing enterocolitis in infants, including examination of the safety database for other similar cases. No study of Venofer® in neonates and infants is requested at this time. However, you should address possible need for and risks involved with Venofer® use in very young pediatric patients;
2. a single-dose, pharmacokinetics study of Venofer® following intravenous administration to adolescent hemodialysis patients on epoetin;
3. an adequate and well-controlled clinical trial of safety and efficacy of Venofer® in the treatment of iron deficiency in children (aged 2 to 12 years) who are on hemodialysis and receive epoetin. (Use of an active control, such as oral iron, or dose ranging comparison should be considered in designing this study.);
4. a study to provide additional safety data (e.g., incidence of allergic or anaphylactic reactions, cross-reactivity with other parenteral iron preparations);
5. develop an *in vitro* release test for Venofer® and propose specifications.

Protocols, data, and final reports should be submitted to your IND for this product and a copy of the cover letter sent to this NDA. If an IND is not required to meet your post marketing commitments, please submit protocols, data and final reports to this NDA as correspondence. In addition, under 21 CFR 314.81(b)(2)(vii), we request that you include a status summary of each commitment in your annual report to this NDA. The status summary should include the number of patients entered in each study, expected completion and submission dates, and any changes in plans since the last annual report. For administrative purposes, all submissions, including labeling supplements, relating to these post marketing commitments must be clearly designated "Post Marketing Commitments."

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

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In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Please submit one market package of the drug product when it is available.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Brian Strongin, Project Manager, at (301) 827-7310.

Sincerely,

Lilia Talarico, M.D.
Director
Division of Gastrointestinal and Coagulation
Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosure

APPEARS THIS WAY
ON ORIGINAL