DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 21135/S-024

SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING REQUIREMENTS

Luitpold Pharmaceuticals, Inc.
Attention: Marsha E. Simon
Manager, Clinical Regulatory Affairs
800 Adams Avenue, Suite 100
Norristown, PA 19403

Dear Ms. Simon:

Please refer to your Supplemental New Drug Application (sNDA) dated September 6, 2011, received September 7, 2011, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Venofer® (Iron Sucrose Injection, USP), 20 mg/mL.

We acknowledge receipt of your amendments dated September 7, 30, October 3, November 1 (3), 14, December 20, 21, 2011 and February 7, 8, March 21, April 6 (2), 13, 19, 27 (2), May 31, June 26, July 23, 30, and September 4, 13, 19, 2012.

We further acknowledge receipt of your communications dated April 16 and December 17, 2010 containing final reports for PMR 852-1, PMC 428-3, PMR 428-6, and PMR 852-2 listed in our November 6, 2000 and June 17, 2005 approval letters.

This "Prior Approval" supplemental new drug application provides for a new patient population, new dosing regimen and final reports for Study IVEN03017 and Study IVEN5033 in fulfillment of PREA postmarketing requirements for the approved Venofer® (Iron Sucrose Injection, USP), 20 mg/mL indications.

We have completed our review of this supplemental application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

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), 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 titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications 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 MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, 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).

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 age 2 years because necessary studies are impossible or highly impracticable. This is because there are too few children with the disease condition to study.

We note that you have fulfilled the pediatric study requirement for ages 2 to 16 years for this application.

FULFILLMENT OF POSTMARKETING REQUIREMENTS/COMMITMENT

We have received your submission dated September 7, 2011, containing the final reports for the following postmarketing commitment and postmarketing requirements listed in the November 6, 2000 and June 17, 2005 approval letters.

PMC 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 an oral iron, or dose ranging comparison should be considered in designing this study).

Final Report Submission: December 17, 2010
(This PMC was subsequently renumbered as PMC 428-3))

PMR 1 Deferred pediatric study under PREA for a pharmacokinetic study of Venofer administration to adolescent non-dialysis-dependent chronic kidney disease (NDD-CKD) patients greater than or equal to 12 years to less than 16 years of age, receiving or not receiving erythropoietin.

Final Report Submission: April 16, 2010
(This PMR was subsequently renumbered as PMR 852-1)

PMR 2 Deferred pediatric study under PREA for the treatment of iron deficiency anemia in non-dialysis-dependent chronic kidney disease (NDD-CKD) pediatric patients ages greater than or equal to two years to less than 12 years receiving or not receiving erythropoietin.

Final Report Submission: December 17, 2010.
(This PMR was subsequently renumbered as PMR 852-2)

We refer to our letter dated November 30, 2005, which deferred all of the pending PMRs until December 31, 2010 and acknowledged the following PREA PMR.

PMR 1 Deferred pediatric study under PREA for the treatment of *iron deficiency anemia [sic]*for hemodialysis dependent-chronic kidney disease (HDD-CKD) patients receiving an erythropoietin in pediatric patients.

Final Report Submission: December 17, 2010
(This PMR was subsequently renumbered as PMR 428-6)

We have reviewed your submissions and conclude that the above requirements were fulfilled. This completes all of your postmarketing requirements and postmarketing commitments acknowledged in our November 6, 2000, June 17, 2005 and November 30, 2005 letters.

POSTMARKETING REQUIREMENTS UNDER 505(o)

Section 505(o)(3) of the FDCA authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute.

Since Venofer® (Iron Sucrose Injection, USP), 20 mg/mL was approved on November 6, 2000, we have become aware of a lack of long term safety data in pediatric patients with chronic kidney disease on erythropoietin-stimulating agent (ESA) therapy who require iron maintenance treatment for iron deficiency anemia. We consider this information to be “new safety information” as defined in section 505-1(b)(3) of the FDCA.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to identify the unexpected serious risk of possible long-term safety in pediatric patients with chronic kidney disease requiring maintenance Venofer® (Iron Sucrose Injection, USP), 20 mg/mL therapy for iron deficiency anemia

Furthermore, the new pharmacovigilance system that FDA is required to establish under section 505(k)(3) of the FDCA will not be sufficient to assess this serious risk.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following:

PMR-1. Observational study to collect long-term safety data in at least 50 pediatric patients with chronic kidney disease on erythropoietin-stimulating agent (ESA) therapy who require iron maintenance treatment for iron deficiency anemia.

The timetable you submitted on September 13, 2012 states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	09/2012
Final Protocol Submission:	09/2013
Study Completion:	12/2016
Final Report Submission:	06/2017

Submit the protocol to your IND 057103 with a cross-reference letter to this NDA. Submit the final report to your NDA. Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate: **"Required Postmarketing Protocol Under 505(o)", "Required Postmarketing Final Report Under 505(o)", "Required Postmarketing Correspondence Under 505(o)"**.

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B of the FDCA, as well as 21 CFR 314.81(b)(2)(vii) requires you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

FDA will consider the submission of your annual report under section 506B and 21 CFR 314.81(b)(2)(vii) to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in 505(o) and 21 CFR 314.81(b)(2)(vii). We remind you that to comply with 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to submit an annual report for studies or clinical trials required under 505(o) on the date required will be considered a violation of FDCA section 505(o)(3)(E)(ii) and could result in enforcement action.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) to:

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

You must submit final promotional materials and package insert(s), 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 http://www.fda.gov/opacom/morechoices/fdaforms/cder.html; instructions are provided on page 2 of the form. 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 Jessica Boehmer, Regulatory Project Manager, at (301) 796-5357.

Sincerely,

{See appended electronic signature page}

Robert C. Kane, M.D.
Deputy Director for Safety
Division of Hematology Products
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

ENCLOSURE:
Content of Labeling

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

/s/

ROBERT C KANE
09/21/2012