CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

205874Orig1s000

Trade Name:	Ferric Citrate 210 mg tablets
Generic Name:	ferric citrate
Sponsor:	Keryx Biopharmaceuticals, Inc.
Approval Date:	September 5, 2014
Indication:	For the control of serum phosphorus levels in patients with chronic kidney disease on dialysis.

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APPROVAL LETTER

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 205874

NDA APPROVAL

Keryx Biopharmaceuticals, Inc.
Attention: James Oliviero, CFA
Chief Financial Officer
750 Lexington Avenue, 20th Floor
New York, NY 10022

Dear Mr. Oliviero:

Please refer to your New Drug Application (NDA) dated August 7, 2013, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for ferric citrate tablets 210 mg.

We acknowledge receipt of your amendments dated August 20, 21, 30, October 3, 4, 9, 24, November 4, 12, 14, 18, 25, December 5, 11 and 12, 2013, and January 9, 10, 17 (2), 24 (2), 28 (2), February 5, 7 (2), 14, March 4, 18, 19, 21 (2), 24, 28 (3), April 1, 2, 3 (2), 4, 11 (2), 18, 22, 23, 28 (2), May 12, 15, 19, 20, 27, 28, June 2, July 1, 14, 31, August 26 and 28, 2014.

This new drug application provides for the use of ferric citrate tablets for the control of serum phosphorus levels in patients with chronic kidney disease on dialysis.

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 text.

A (b) (4) retest date is granted for the drug substance (b) (4) An 18-month shelf-life is granted for the tablets packaged in the proposed commercial package and stored at controlled room temperature.

Please note that the dissolution results of two out of three registration batches significantly failed the dissolution acceptance criteria at the 24-month stability time point. In the future, if you request a shelf-life extension for the tablets beyond the granted expiry dating of 18 months, the request should be submitted as a supplement, not as a change in an annual report.

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. 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

Submit final printed carton and immediate container labels that are identical to the enclosed carton and immediate container labels as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (June 2008)*. Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved NDA 205874**." Approval of this submission by FDA is not required before the labeling is used.

Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

ADVISORY COMMITTEE

Your application for ferric citrate was not referred to an FDA advisory committee because the application did not raise significant safety or efficacy issues that were unexpected for a drug/biologic of this class.

PROPRIETARY NAME

If you intend to have a proprietary name for this product, the name and its use in the labels must conform to the specifications under 21 CFR 201.10 and 201.15. We recommend that you submit a request for a proposed proprietary name review. (See the guidance for industry *Contents of a Complete Submission for the Evaluation of Proprietary Names*, available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm075068.pdf and "PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2008 through 2012".)

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 birth to six months because there is evidence strongly suggesting that the drug product would be unsafe in this pediatric group. Data from animal studies indicate that greater gastrointestinal toxicity was observed when ferric citrate was administered by gavage and less toxicity was observed when it was administered with solid food. As patients under 6 months of age are unlikely to be eating solid food, they may be at greater risk of gastrointestinal toxicity.

We are deferring submission of your pediatric study for ages six months to < 18 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. This required study is listed below.

2104-1 A multi-center clinical trial to evaluate the dosing and safety of ferric citrate for the treatment of hyperphosphatemia in children ages six months to < 18 years with chronic kidney disease

Final Protocol Submission:	8/31/15
Study Completion:	6/30/19
Final Report Submission:	12/31/19

Submit the protocol to your IND 52868, 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.

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).

MEDWATCH-TO-MANUFACTURER PROGRAM

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this

product. To participate in the program, please see the enrollment instructions and program description details at http://www.fda.gov/Safety/MedWatch/HowToReport/ucm166910.htm.

If you have any questions, please call Russell Fortney, Regulatory Project Manager, at (301) 796-1068.

Sincerely,

{See appended electronic signature page}

Norman Stockbridge, M.D., Ph.D.
Director
Division of Cardiovascular and Renal Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosures:
Content of Labeling
Carton and Container Labeling

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

/s/

NORMAN L STOCKBRIDGE
09/05/2014