

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-180

APPROVAL LETTER



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-180

NDA APPROVAL

AMAG Pharmaceuticals, Inc
Attention: Mohammed Salem, Ph.D., RAC
100 Hayden Avenue
Lexington, MA 02421

Dear Dr. Salem:

Please refer to your new drug application (NDA) dated December 18, 2007, received December 19, 2007, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Feraheme™ (ferumoxytol) Injection.

We acknowledge receipt of your submissions dated February 27, April 3, 10, 14 and 28, May 20, June 5 and 23, July 14, 16 and 24, August 4, 5 and 7, September 3 (2), 5, 22 (2), 23, 24 and 25, October 1, 3 and 30, December 17, 2008; January 7, February 10, March 20 and 30, April 8, 14 and 29 (2), May 5 and 26, June 4, 9, 10, 16 and 18, 2009.

The April 29, 2009, submission constituted a complete response to our December 22, 2008, action letter.

This new drug application provides for the use of Feraheme™ (ferumoxytol) Injection for the treatment of iron deficiency anemia in adult patients with chronic kidney disease (CKD).

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.

PEDIATRIC RESEARCH EQUITY ACT (PREA)

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We are waiving the pediatric study requirement for ages 0 to < 2 years and deferring pediatric studies for ages 2 to < 18 years for this application.

Your deferred pediatric studies required under section 2 of the Pediatric Research Equity Act (PREA) are considered required postmarketing requirements. The statuses of these postmarketing studies shall be reported annually according to 21 CFR 314.81. These requirements are listed below.

1. To conduct a clinical trial in pediatric patients aged 2 to < 18 years who have iron deficiency anemia and who are receiving either hemodialysis or peritoneal dialysis. In addition to any

other items, the trial will obtain pharmacokinetic (PK), pharmacodynamic (PD) and safety data from at least 50 patients exposed to ferumoxytol. In this trial, patients will be randomized to oral iron (25 patients) or one of two dose ferumoxytol dose regimens (25 patients in each dose cohort). Endpoints will consist of PK, PD, comparisons of hemoglobin changes and safety summaries.

The timetable you submitted on June 9, 2009, states that you will conduct this study according to the following timetable:

Final clinical protocol submission date:	December 2009
Clinical trial completion date:	April 2013
Final trial report submission date:	October 2013

2. To conduct a clinical trial in pediatric patients aged 2 to < 18 years who have iron deficiency anemia and chronic kidney disease that does not require dialysis. In addition to any other items, the trial will obtain pharmacokinetic (PK), pharmacodynamic (PD) and safety data from at least 50 patients exposed to ferumoxytol. In this trial, patients will be randomized to oral iron (25 patients) or one of two dose ferumoxytol dose regimens (25 patients in each dose cohort). Endpoints will consist of PK, PD, comparisons of hemoglobin changes and safety summaries.

The timetable you submitted on June 9, 2009, states that you will conduct this study according to the following timetable:

Final clinical protocol submission date:	December 2009
Clinical trial completion date:	April 2013
Final trial report submission date:	October 2013

Submit final study reports to this NDA. For administrative purposes, all submissions related to these pediatric postmarketing study requirements must be clearly designated "**Pediatric Study Requirements**".

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format as described at <http://www.fda.gov/oc/datacouncil/spl.html> that is identical to the enclosed labeling (text for the package insert) and/or submitted labeling (package insert submitted June 18, 2009). Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission, "SPL for approved NDA 22-180."

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels that are identical to the enclosed carton and immediate container labels and/or submitted 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 titled *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (October 2005)*. 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 22-180.**” 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.

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(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
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(s), at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see www.fda.gov/cder/ddmac.

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

LETTERS TO HEALTH CARE PROFESSIONALS

If you issue a letter communicating important safety related information about this drug product (i.e., a “Dear Health Care Professional” letter), we request that you submit an electronic copy of the letter to both this NDA and to the following address:

MedWatch
Food and Drug Administration
Suite 12B05
5600 Fishers Lane
Rockville, MD 20857

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 Hyon-Zu Lee, Pharm.D., Regulatory Project Manager, at 301-796-2050.

Sincerely,

{See appended electronic signature page}

Rafel Dwaine Rieves, M.D.
Director
Division of Medical Imaging and Hematology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research

Enclosure

**This is a representation of an electronic record that was signed electronically and
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/s/

Rafel Rieves
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