DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 22180/S-011
NDA 22180/S-013

SUPPLEMENT APPROVAL

AMAG Pharmaceuticals, Inc.
Attention: Alka Batycky, Ph.D.
Vice President, Clinical Operations,
Regulatory Affairs, Program and Alliance Management
1100 Winter Street
Waltham, MA 02451

Dear Dr. Batycky:

Please refer to your Supplemental New Drug Application (sNDA), Supplement-011, dated June 6, 2014, received June 6, 2014, and your Supplemental New Drug Application (sNDA), Supplement-013 dated February 12, 2015, received February 12, 2015 both submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Feraheme® (ferumoxytol) Injection, 510 mg.

We acknowledge receipt of your amendments to Supplement-011 dated December 2, 2014; and March 4, 5, 9, and 10, 2015.

We also acknowledge receipt of your amendments to Supplement-013 dated March 4, 5, 9, and 10, 2015.

We also refer to our letter dated January 7, 2015, notifying you, under Section 505(o)(4) of the FDCA, of new safety information that we believe should be included in the labeling for Feraheme® (ferumoxytol). This information pertains to the risk of serious hypersensitivity reactions including anaphylaxis and death occurring during and closely following the administration of Feraheme® (ferumoxytol).

This supplemental new drug application, Supplement-013 provides for revisions to the labeling for Feraheme® (ferumoxytol), consistent with our January 7, 2015 Safety Labeling Change Notification Letter.

1. A description of the risks of serious hypersensitivity/anaphylaxis reactions in a Boxed Warning in addition to the existing information in the Warnings and Precautions section
2. Revisions to the administration procedure to describe that Feraheme should only be administered as an intravenous infusion in 50-200 ml of 0.9% sterile sodium chloride or

5% sterile dextrose over a minimum period of 15 minutes following dilution, and deletion of the option for direct injection of the undiluted product

3. Add advice that patients should be closely monitored for signs and symptoms of hypersensitivity reactions, including monitoring of blood pressure and pulse during administration and for at least 30 minutes following each infusion of Feraheme
4. Add advice that Elderly patients (> 65 years of age) or patients with multiple co-morbidities who experience a serious hypersensitivity reaction due to Feraheme may have more severe outcomes. The potential risks and benefits of Feraheme administration should be carefully considered in these patients.

The agreed upon changes to the language included in our January 7, 2015 Safety Labeling Change Notification letter are as follows (additions are noted by underline and deletion are noted by ~~strikethrough~~).

HIGHLIGHTS OF PRESCRIBING INFORMATION

---RECENT MAJOR CHANGES---

(b) (4)

WARNING RISK FOR SERIOUS HYPERSENSITIVITY/ANAPHYLAXIS REACTIONS
See full prescriber information for complete boxed warning.

Fatal and serious hypersensitivity reactions including anaphylaxis have occurred in patients receiving Feraheme. Initial symptoms may include hypotension, syncope, unresponsiveness, cardiac/cardiorespiratory arrest.

- **Only administer Feraheme when personnel and therapies are immediately available for the treatment of anaphylaxis and other hypersensitivity reactions (5.1)**
- **Observe for signs or symptoms of hypersensitivity reactions during and for at least 30 minutes following Feraheme infusion including monitoring of blood pressure and pulse during and after Feraheme administration (5.1)**
- **Hypersensitivity reactions have occurred in patients in whom a previous Feraheme dose was tolerated (5.1)**

------DOSAGE AND ADMINISTRATION----

- The recommended dose of Feraheme is an initial 510 mg dose followed by a second 510 mg dose 3 to 8 days later.
- Administer Feraheme as ~~an undiluted intravenousinjection delivered at a rate of up to 1 mL/sec (30 mg/sec), or as~~ an intravenous infusion in 50-200 mL 0.9% Sodium Chloride Injection, USP or 5% Dextrose Injection USP over at least 15 minutes.

----DOSAGE FORMS AND STRENGTHS---

Injection: 510 mg iron/17 mL (30 mg/mL) in single use vials. (3)

9 Pages Of Draft Labeling Have Been Withheld In Full As b4 (CCI/TS) Immediately Following This Page

General information about the safe and effective use of Feraheme.
Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. If you would like more information, talk to your healthcare provider. You can ask your pharmacist or healthcare provider for information about Feraheme that is written for health professionals.

What are the ingredients in Feraheme?
Active ingredient: ferumoxytol
Inactive ingredient: mannitol
Distributed by: AMAG Pharmaceuticals, Inc. Waltham, MA 02451 Manufactured by: Pa heon Manufacturing Services LLC, Greenville, NC
For more information, go to www.feraheme.com or call 1--877-411-2510.

This Patient Information has been approved by the U.S. Food and Drug Administration Issued: Mar/2015

APPROVAL & LABELING

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, text for the patient 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 that includes 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 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.

Because none of these criteria apply to your application, you are exempt from this requirement.

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/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.

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 package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the address above or by fax to 301-847-8444.

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 Ms. Jessica Boehmer, Regulatory Project Manager, at (301) 796-5357.

Sincerely,

{See appended electronic signature page}

Robert C. Kane, MD
Deputy Director for Safety
Division of Hematology Products
Office of Hematology 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
03/16/2015