



NDA 22180/S-006

SUPPLEMENT APPROVAL

AMAG Pharmaceuticals, Inc.
Attention: Ratna Lingamaneni, Ph.D., RAC
Director, Regulatory Affairs
100 Hayden Avenue
Lexington, MA 02421

Dear Dr. Lingamaneni:

Please refer to your Supplemental New Drug Application (sNDA) dated May 10, 2011, received May 10, 2011, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Feraheme[®] (ferumoxytol) Injection, 30 mg/mL.

We acknowledge receipt of your amendment dated June 20, 2011.

This “Prior Approval” supplemental new drug application proposes to decrease the post-dose observation period from 60 minutes to 30 minutes, and provides the following revisions to the labeling for Feraheme[®] (ferumoxytol) Injection:

1. In the **HIGHLIGHTS OF PRESCRIBING INFORMATION**, under **RECENT MAJOR CHANGES**, the following bullet was added:

“• Warnings and Precautions (5.1) 6/2011”

2. In the **HIGHLIGHTS OF PRESCRIBING INFORMATION**, under the **WARNINGS AND PRECAUTIONS** section, the first bullet that begins with “Hypersensitivity Reactions: . . .” was revised to read:

“• Hypersensitivity Reactions: Observe for signs and symptoms of hypersensitivity during and after Feraheme administration for at least 30 minutes and until clinically stable following completion of each administration. (5.1).”

3. In the **FULL PRESCRIBING INFORMATION**, the **5.1 HYPERSENSITIVITY REACTIONS** section was revised as follows (with bolded text as shown):

“Serious hypersensitivity reactions, including anaphylactic-type reactions, some of which have been life-threatening and fatal, have been reported in patients receiving Feraheme. Observe patients for signs and symptoms of hypersensitivity during and after Feraheme administration for at least 30 minutes and until clinically stable

following completion of each administration. Only administer the drug when personnel and therapies are immediately available for the treatment of anaphylaxis and other hypersensitivity reactions [see Adverse Reactions (6.1)]. Anaphylactic-type reactions presenting with cardiac/cardiorespiratory arrest, clinically significant hypotension, syncope, and unresponsiveness have been reported in the post-marketing experience [see Adverse Reactions from Post-marketing Spontaneous Reports (6.2)]. In clinical studies, serious hypersensitivity reactions were reported in 0.2% (3/1,726) of subjects receiving Feraheme. Other adverse reactions potentially associated with hypersensitivity (e.g., pruritus, rash, urticaria or wheezing) were reported in 3.7% (63/1,726) of these subjects.”

4. In the **FULL PRESCRIBING INFORMATION**, in the **1 INDICATIONS AND USAGE** section, the text for the pharmacologic class that reads “an iron replacement product” was deleted. The section was revised to read as follows:

“Feraheme is indicated for the treatment of iron deficiency anemia in adult patients with chronic kidney disease (CKD).”

5. In the **FULL PRESCRIBING INFORMATION**, in the **4 CONTRAINDICATIONS** section, the following bullets were deleted:
- Evidence of iron overload
 - Anemia not caused by iron deficiency”
6. In the **FULL PRESCRIBING INFORMATION**, in the **5.3 IRON OVERLOAD** section, the text “[see *Contraindications (4)*]” was deleted.
7. In the **FULL PRESCRIBING INFORMATION**, in the **6.2 ADVERSE REACTIONS FROM POST-MARKETING SPONTANEOUS REPORTS** section, the text “anaphylactoid” was replaced with “anaphylactic-type.”
8. In the **FULL PRESCRIBING INFORMATION**, in the **10 OVERDOSAGE** section, the text “[see *Contraindications (4)*]” was replaced with “[*Warnings and Precautions (5.3)*].”

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, except with the revisions listed, 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 via 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 with the revisions indicated above approved in this supplemental application, as well as annual reportable changes, and annotate each change.

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
Division of Drug Marketing, Advertising, and Communications
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 Division of Drug Marketing, Advertising, and Communications (DDMAC), 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, contact Trinh Scott, Regulatory Project Manager, at (301) 796-3311 or Trinh.Scott@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Robert Kane, M.D.
Deputy Division Director for Safety (Acting)
Division of Hematology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research
Food and Drug Administration

ENCLOSURE(S):
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
06/21/2011