

**TRANSMITTED BY FACSIMILE**

Linda S. Pollitz, RAC
Director, Regulatory Affairs
AMAG Pharmaceuticals, Inc.
100 Hayden Avenue
Lexington, MA 02421

RE: NDA 022180
Feraheme[®] (ferumoxytol) Injection For Intravenous (IV) use
MACMIS #19575

Dear Ms. Pollitz:

The Division of Drug Marketing, Advertising, and Communications (DDMAC) of the U.S. Food and Drug Administration (FDA) has reviewed a professional "Direct Mail-Nephrology" (AMAG P/N DR-0266-0810) [Nephrology direct mailer] for Feraheme[®] (ferumoxytol) Injection For Intravenous (IV) use (Feraheme) submitted by AMAG Pharmaceuticals, Inc. (AMAG) under cover of Form FDA 2253. The Nephrology direct mailer is misleading because it overstates the efficacy of Feraheme. Thus, the Nephrology direct mailer misbrands the drug in violation of the Federal Food, Drug, and Cosmetic Act (the Act), 21 U.S.C. 352(a) and FDA's implementing regulations. *Cf.* 21 CFR 202.1(e)(6)(i) & (e)(7)(i).

Background

According to its FDA-approved product labeling (PI):

Feraheme[®] (ferumoxytol) Injection is indicated for the treatment of iron deficiency anemia in adult patients with chronic kidney disease (CKD).

The safety and efficacy of Feraheme were assessed in three randomized, open-label, controlled clinical trials (Trials 1, 2 and 3). The primary efficacy endpoint for these trials was the change in hemoglobin from baseline to day 35. Secondary endpoints included: the percentage of patients who were hemoglobin responders at day 35; the mean change from baseline in serum ferritin at day 21; and the mean change from baseline in transferrin saturation (TSAT) (%) at day 35. In all three studies, patients with CKD and iron deficiency anemia were randomized to treatment with Feraheme or oral iron.

Overstatement of Efficacy

Promotional materials are misleading if they represent or suggest that a drug is more effective than has been demonstrated by substantial evidence or substantial clinical experience. The direct mailer includes the following claims and presentations:

- “Hgb rise without ESA?”
- “Feraheme increases Hgb [hemoglobin], even without an ESA”
- “Greater increases in Hgb vs oral iron in non-dialysis dependent (NDD) CKD patients, independent of ESAs¹”
- “Mean change in Hgb (the primary efficacy endpoint) from baseline by ESA use at Day 35 in non-dialysis patients¹” accompanied by two bar graphs that depict mean changes in hemoglobin from baseline to day 35, stratified by concomitant ESA use, in the Feraheme and oral iron treatment groups.

This presentation misleadingly overstates the efficacy of Feraheme by suggesting that increases in hemoglobin levels have been demonstrated specifically in patients without concomitant ESA use when this finding has not been demonstrated by substantial evidence or substantial clinical experience. The three pivotal trials used to evaluate the clinical efficacy of Feraheme were all designed to measure the change in hemoglobin from baseline to day 35 across the respective study populations as a whole. While concomitant ESA use at baseline was noted, none of the studies, including the referenced trial, were designed to evaluate the efficacy of Feraheme based on ESA use and patients were not stratified by ESA use at randomization. Therefore, conclusions based on this sub-group analysis are considered exploratory and do not constitute substantial evidence to support any benefit or efficacy claims for this subgroup. This misleading impression is further exacerbated by the complete omission of the results of the actual primary efficacy analyses from these studies.

Conclusion and Requested Action

For the reasons discussed above, the Nephrology direct mailer misbrands Feraheme in violation of the Act, 21 U.S.C. 352(a) and FDA’s implementing regulations. Cf. 21 CFR 202.1 (e)(6)(i) & (e)(7)(i).

DDMAC requests that AMAG immediately cease the dissemination of violative promotional materials for Feraheme such as those described above. Please submit a written response to this letter on or before March 4, 2011, stating whether you intend to comply with this request, listing all promotional materials (with the 2253 submission date) for Feraheme that contain violations such as those described above, and explaining your plan for discontinuing use of such violative materials. Please direct your response to me at the 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, facsimile at 301-847-8444. In all future correspondence regarding this matter, please refer to MACMIS #19575 in addition to the NDA number. We remind you that only written communications are considered official.

¹ Spinowitz BS, Kausz AT, Baptista J, Noble SD, Sothinathan R, Bernardo MV, Brenner L, Pereira BJJ. Ferumoxytol for treating iron deficiency anemia in CKD. *Journal of the American Society of Nephrology*. 2008; 19(8): 1599-1605

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to ensure that your promotional materials for Feraheme comply with each applicable requirement of the Act and FDA implementing regulations.

Sincerely,

{See appended electronic signature page}

James S. Dvorsky, PharmD
Regulatory Review Officer
Division of Drug Marketing,
Advertising, and Communications

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

/s/

JAMES S DVORSKY
02/17/2011