DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

TRANSMITTED BY FACSIMILE

Linda Kunka
Regulatory Affairs Associate
Watson Pharmaceuticals, Inc.
360 Mt. Kemble Avenue
P.O. Box 1953
Morristown, NJ 07962

Re: NDA # 20-955
Ferrlecit (sodium ferric gluconate complex in sucrose injection)
MACMIS # 13009

Dear Ms. Kunka:

The Division of Drug Marketing, Advertising, and Communications (DDMAC) has reviewed a reminder ad (FER4029) and a non-product specific belly band (FER4042) for Ferrlecit (sodium ferric gluconate complex in sucrose injection) that appeared on the outside back cover and around the October 2004, edition of *Kidney International* October 2004 vol 66(4) and was submitted by Watson Pharmaceuticals, Inc. (Watson) under cover of Form FDA 2253. The agency considers these two pieces, which share numerous presentation elements and are presented in direct conjunction with one another, to be a full product ad for Ferrlecit. This full product ad is false or misleading because it fails to disclose the drug's indication, fails to present any risk information for Ferrlecit, and contains an unsubstantiated claim. This ad thus misbrands Ferrlecit in violation of the Federal Food, Drug, and Cosmetic Act (Act), 21 U.S.C. § 352(n), and FDA's implementing regulations, 21 CFR 202.1(e)(1); (e)(3)(ii); & (e)(6)(i).

Background

According to the FDA-approved labeling (PI), Ferrlecit is a hematinic agent indicated for treatment of iron deficiency anemia in patients undergoing chronic hemodialysis who are receiving supplemental epoetin therapy.

The "Contraindications" section of the PI states, in part:

- All anemias not associated with iron deficiency.
- Evidence of iron overload.

Furthermore, the "Warnings" section of the PI states:

> Hypersensitivity reactions have been reported with injectable iron products.

The PI lists other risk information associated with use of Ferrlecit, including, but not limited to, the following statements in the "Precautions" section:

> *General:*
> Iron is not easily eliminated from the body and accumulation can be toxic. Unnessesary therapy with parenteral iron will cause excess storage of iron with consequent possibility of iatrogenic hemosiderosis. Iron overload is particularly apt to occur in patients with hemoglobinopathies and other refractory anemias.
>
> *Hypersensitivity Reactions:*
> Serious hypersensitivity reactions have been reported rarely in patients receiving Ferrlecit. One case of a life-threatening hypersensitivity reaction has been observed in 1,097 patients who received a single dose of Ferrlecit in a post-marketing safety study. Three serious hypersensitivity reactions have been reported from the spontaneous reporting system in the United States.
>
> *Hypotension:*
> Hypotension associated with light-headedness, malaise, fatigue, weakness or severe pain in the chest, back, flanks, or groin has been associated with administration of intravenous iron. These hypotensive reactions are not associated with signs of hypersensitivity and have usually resolved within one or two hours.

According to the “Adverse Reactions” section of the PI, Ferrlecit is associated with hypotension, nausea, vomiting and/or diarrhea, pain, hypertension, allergic reaction, chest pain, pruritis, and back pain.

Omission of Indication and Risk Information

The reminder ad and belly band share numerous presentation elements (e.g., same font, same background, use of color, and company logo) with one another and were placed in direct physical proximity to one another. Specifically, the belly band was placed around *Kidney International* October 2004 vol 66(4) issue. The Ferrlecit reminder ad was on the outside back cover of the same edition of *Kidney International.* Placement of these two pieces, sharing numerous presentation elements and in direct conjunction with each other creates a full product ad.

Additionally, the belly band, while not specifically naming Ferrlecit, represents or suggests it is an advertisement for this product by its inclusion of a dose of 12.5 mg/min. While there are currently three types of IV iron products available for use in the U.S, the dosing for each product is very specific. Only Ferrlecit has this dosing characteristic.

The combined piece makes several representations or suggestions about Ferrlecit, including the following on the belly band:

- Deliver IV iron where it's needed
- Effective iron mobilization
- Regulated iron delivery
- IV push can be administered at 12.5 mg/min

However, the ad omits the specific indication for the drug and fails to include any risk information for the drug, including important contraindications, warnings, precautions, and adverse reactions, as required by 21 U.S.C. § 352(n) and FDA's implementing regulations. See 21 CFR 202.1(e)(1) & (e)(3)(ii).

Unsubstantiated Claim

The belly band includes the claim "Easy administration." This claim is misleading at best. According to the "Dosage and Administration" section of the PI for Ferrlecit, most patients will require that the drug be administered (intravenously) over eight sessions at sequential dialysis treatments in order to achieve a favorable hemoglobin or hematocrit response. Furthermore, patients may need to continue therapy at the lowest dose necessary to maintain target levels of hemoglobin, hematocrit, and laboratory parameters of iron storage within acceptable limits. This type of assessment would require laboratory monitoring. In addition, patients need to be monitored for potential hypotensive reactions with the infusion. See 21 CFR 202.1(e)(6)(i).

Conclusion and Requested Action

Your ad makes claims for Ferrlecit, but fails to disclose any risk information, fails to disclose the drug's indication, and makes an unsubstantiated claim. Accordingly, these promotional pieces misbrand Ferrlecit in violation of section 502(n) of the Act, 21 U.S.C. § 352(n), and FDA's implementing regulations. See 21 CFR 202.1(e)(1); (e)(3)(ii); & (e)(6)(i).

DDMAC requests that Watson immediately cease the dissemination of promotional materials for Ferrlecit with the same or similar claims as those described above. Please submit a written response to this letter on or before May 19, 2005, describing your intent to comply with this request, listing all promotional materials for Ferrlecit with the same or similar claims as those described above, and explaining your plan for discontinuing use of such materials. Please direct your response to me at the Food and Drug Administration, Division of Drug Marketing, Advertising, and Communications, HFD-42, Rm. 8B-45, 5600 Fishers Lane, Rockville, Maryland 20857, facsimile at 301-594-6771. In all future correspondence regarding this matter, please refer to MACMIS ID # 13009 in addition to the NDA number. We remind you that only written communications are considered official. If you choose to revise your promotional materials, DDMAC is willing to assist you in assuring that your revised materials comply with applicable provisions of the Act by reviewing your revisions before you use them in promotion.

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

Sincerely,

{See appended electronic signature page}

Shannon R. Benedetto, Pharm.D., M.B.A.
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/

Shannon Benedetto
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