



Felicia A. Bullock  
Senior Director, Regulatory Affairs  
Luitpold Pharmaceuticals, Inc.  
One Luitpold Drive  
PO Box 9001  
Shirley, New York 11967

**RE: NDA #203565**  
Injectafer<sup>®</sup> (ferric carboxymaltose injection)  
MA #34

Dear Ms. Bullock:

The Office of Prescription Drug Promotion (OPDP) of the U.S. Food and Drug Administration (FDA) has reviewed the Balancing Act Video Segment (FCM061) (video segment)<sup>1</sup> for Injectafer<sup>®</sup> (ferric carboxymaltose injection) (Injectafer), submitted by Luitpold Pharmaceuticals, Inc. (Luitpold) under cover of Form FDA-2253. The video segment provides evidence that Injectafer is intended for a new use for which it lacks approval, and for which its labeling does not provide adequate directions, which renders Injectafer misbranded within the meaning of the Federal Food, Drug, and Cosmetic Act (FD&C Act) and makes its distribution violative. See 21 U.S.C. 355(a); 352(f); 331(a), (d); 21 CFR 201.5; 201.100; 201.115; 201.128. In addition, the video segment is false or misleading because it minimizes important risk information associated with the drug, omits material facts, and makes misleading claims. Thus, the video segment misbrands Injectafer within the meaning of the FD&C Act, and makes its distribution violative. See 21 U.S.C. 352(a), (n); 321(n); 331(a); 21 CFR 1.21(a); 202.1(e)(5)(i), (iii).

## Background

Below are the indication and summary of the most serious and common risks associated with the use of Injectafer.<sup>2</sup> According to the INDICATIONS AND USAGE section of the FDA-approved Injectafer product labeling (PI):

Injectafer is indicated for the treatment of iron deficiency anemia in adult patients:

- who have intolerance to oral iron or have had unsatisfactory response to oral iron;
- who have non-dialysis dependent chronic kidney disease.

<sup>1</sup> The video is also available on the internet at <http://www.thebalancingact.com/american-regent/> (last accessed January 28, 2015).

<sup>2</sup> This information is for background purposes only and does not necessarily represent the risk information that should be included in the promotional piece cited in this letter.

Injectafer is contraindicated in patients with hypersensitivity to Injectafer or any of its components.

Injectafer is associated with a number of serious risks. The PI contains Warnings and Precautions regarding hypersensitivity reactions, hypertension, and laboratory test alterations. The most common adverse reactions in patients receiving Injectafer were nausea, hypertension, flushing, hypophosphatemia, and dizziness.

### **Lack of Adequate Directions for Use**

The video segment presents the following claims in the main audio portion:

- “In the United States, an estimated 7.5 million people suffer from iron deficiency anemia or IDA and well over one third of those with IDA are women and children.”
- “Well, it's called Injectafer, or ferric carboxymaltose. It's the first IV iron approved in the U.S. for patients with iron deficiency anemia caused by any disease. In fact, it's also for patients who are intolerant to oral iron or where oral iron is unsatisfactory and it's also approved in adult patients in non-dialysis chronic kidney disease.”

These claims are misleading because they suggest that Injectafer is used to treat **all** patients, including children, with iron deficiency anemia (IDA), regardless of concomitant disease or prior treatment, **in addition to** the two limited subsets of patients specified later in the claim. However, Injectafer's indication is limited to second line treatment in adult IDA patients who have an intolerance or unsatisfactory response to oral iron, or to patients who have non-dialysis dependent chronic kidney disease. The approved labeling for Injectafer does not provide instructions for, or otherwise indicate that Injectafer will be safe and effective for all IDA patients. Information sufficient to demonstrate that Injectafer is safe and effective for these new intended uses has not been submitted to FDA in an application. In sum, these presentations provide evidence that Injectafer is intended for new uses for which it lacks approval, and for which its labeling does not provide adequate directions for use.

### **Minimization of Risk**

The video segment minimizes the risks of Injectafer by failing to convey significant risk information associated with the use of Injectafer. The video segment, hosted by Olga Villaverde (Villaverde), consists of a seven-minute interview featuring a blood specialist, Dr. Tim Goodnough (Goodnough), and a senior manager of marketing at American Regent, Inc.<sup>3</sup>, Lynell D'Sylva (D'Sylva). While the audio portion of the interview discusses IDA and the benefits of Injectafer treatment, it fails to discuss **any** risks associated with Injectafer. Instead, the risk information appears in a super which is displayed on-screen for approximately 30 seconds out of the nearly seven-minute video segment. In addition, the information is difficult to read because it is presented in very small type font, without a contrasting background. Furthermore, the risk information appears at the bottom of the video segment and is displayed at the same time as the audio portion of the interview, which distracts the audience from the risk information. Therefore, this presentation is misleading

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<sup>3</sup> American Regent, Inc. is a division of Luitpold Pharmaceuticals, Inc.

because it fails to provide sufficient emphasis for Injectafer's important risk information in the main part of the video.

The video segment also presents the following dialogue:

Goodnough: "Blood transfusions have been the traditional treatment for iron deficiency anemia...[a]nd blood transfusions are now identified amongst the top five unnecessary therapeutic procedures in the United States and they carry risks. Traditional treatments, such as iron tablet supplementation are very difficult for patients to tolerate and they become non-compliant because of GI [gastrointestinal] side effects and in the past, intravenous iron treatments have been approved at lower doses and only in patients with chronic kidney disease...."

Villaverde: "[D'Sylva], let's talk about this new treatment. What is it?"

D'Sylva: "Well, it's called Injectafer, or ferric carboxymaltose."

This presentation discusses potential risks related to the use of other types of IDA treatments (e.g., blood transfusions and oral iron) but fails to disclose that Injectafer is also associated with many of the same risks. For example, the risks attributed to oral iron in the claim above, including certain GI side effects such as nausea, constipation, abdominal pain, and diarrhea, are also associated with Injectafer use. In fact, in the pivotal trial, some of these side effects (i.e., nausea) actually occurred more frequently in patients taking Injectafer compared to those taking oral iron. The lack of prominent, balancing risk information for Injectafer, as described above, further exacerbates the misleading nature of this presentation.

### **Omission of Material Fact**

Promotional materials are misleading if they fail to reveal facts that are material in light of the representations made by the materials or with respect to consequences that may result from the use of the drug as recommended or suggested in the materials.

In the video segment, D'Sylva claims that Injectafer is "the first FDA-approved iron approved as a high single dose IV iron and a total dose of IV iron." This claim suggests that Injectafer can be administered as a single, high dose of iron, which is inconsistent with the approved dosing and administration instructions for Injectafer. The PI states that Injectafer is to be given "in **two doses separated by at least 7 days**" (emphasis added). Furthermore, according to the Patient Information, "INJECTAFER is administered intravenously (into your vein) by your doctor or health care professional in **two doses**" (emphasis added). Therefore, because the video segment fails to present this important dosing information, the video segment omits material facts. We note that the video segment includes a statement regarding two doses (i.e., "Studies have shown that patients with IDA have deficits on average of 1,500 mg of iron and so two 750 mg doses can correct that."). However, this statement does not clearly indicate the full, recommended dosing regimen for Injectafer, and does not mitigate the misleading impression in the video segment.

## Misleading Claims

The video segment presents the following dialogue:

Villaverde: “Do you have maybe a...patient in your mind that...has taken [Injectafer] and [it] really changed her life, or his life?”

Goodnough: “I think IDA is an unmet medical need and I’ve had elderly patients – I remember one in particular – who was a tea and toast lady living alone, had been losing weight and was diagnosed with IDA and wasn’t able to take the oral iron pills and she blossomed like a rose with high-dose IV iron.”

The above presentation is false or misleading because it suggests that treatment with Injectafer can drastically improve the general well-being of a patient with IDA (*i.e.*, Injectafer “really changed her life” and the patient “blossomed like a rose” with Injectafer). These claims relate to a drug’s positive impact on a patient’s general well-being and misleadingly imply a broad effect of the drug on various aspects of a patient’s life, including *non*-health-related aspects of life.

The video segment also presents the following claims in reference to Injectafer:

Goodnough: In the past, intravenous iron treatments have been approved at lower doses and only in patients with chronic kidney disease...”

...

Villaverde: “And [D’Sylva], from what I am hearing this could really be a huge benefit to so many millions of people that suffer from IDA.”

D’Sylva: “Oh, it’s...transforming the way iron deficiency anemia is treated.”

This presentation is misleading because it implies that Injectafer offers advantages (both therapeutic and non-therapeutic) over other currently approved treatments, when this has not been demonstrated. FDA is not aware of any evidence to support the implication that Injectafer offers significant advantages over other prescription drugs already approved for this condition. Therefore, claims that Injectafer “transform[s] the way iron deficiency anemia is treated” and offers a “huge benefit” to a previously untreated population are misleading. If you have data to support these claims, please submit them to FDA for review.

## Conclusion and Requested Action

The video segment is false or misleading because it minimizes important risk information associated with the drug, omits material facts, and makes misleading claims about the drug. Furthermore, the video segment provides evidence that Injectafer is intended for a new use for which it lacks approval, and for which its labeling does not provide adequate directions. See 21 U.S.C. 355(a); 352(f); 331(a), (d); 21 CFR 201.5; 201.100; 201.115; 201.128. The video segment also misbrands Injectafer within the meaning of the FD&C Act, and makes its distribution violative. See 21 U.S.C. 352(a), (n); 321(n); 331(a); 21 CFR 1.21(a); 202.1(e)(5)(i), (iii).

OPDP requests that Luitpold immediately cease violating the FD&C Act, as discussed above. Please submit a written response to this letter on or before February 12, 2015, stating whether you intend to comply with this request, listing all promotional materials (with the 2253 submission date) for Injectafer that contain statements such as those described above, and explaining your plan for discontinuing use of such materials.

Please direct your response to the undersigned at the **Food and Drug Administration, Center for Drug Evaluation and Research, Office of Prescription Drug Promotion, 5901-B Ammendale Road, Beltsville, Maryland 20705-1266** or by facsimile at (301) 847-8444. To ensure timely delivery of your submissions, please use the full address above and include a prominent directional notation (e.g., a sticker) to indicate that the submission is intended for OPDP. Please refer to MA #34 in addition to the NDA number in all future correspondence relating to this particular matter. All correspondence should include a subject line that clearly identifies the submission as a "Response to Untitled Letter." OPDP reminds you that only written communications are considered official.

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to ensure that your distribution of Injectafer complies with each applicable requirement of the FD&C Act and FDA implementing regulations.

Sincerely,

{See appended electronic signature page}

James S. Dvorsky, PharmD  
Regulatory Review Officer  
Office of Prescription Drug Promotion

{See appended electronic signature page}

Kathleen Davis  
Team Leader  
Office of Prescription Drug Promotion

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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JAMES S DVORSKY  
01/29/2015

KATHLEEN T DAVIS  
01/29/2015