

Questions

1. (Vote) Injectafer is proposed for use in the treatment of iron deficiency anemia among postpartum patients (PP) and patients with heavy uterine bleeding (HUB), including patients who might otherwise receive treatment with oral iron. Oral iron was the control treatment within most randomized clinical studies, although some studies compared Injectafer to Venofer or a placebo. Of concern were numerical imbalances in adverse events, including mortality, as follows:

Mortality		
Group	Injectafer	Control
All randomized, multicenter studies	5/1206 (0.4%)	1/994* (0.1%)
Randomized, multicenter, oral-iron controlled studies	4/1057 (0.4%)	0/834 (0%)

*oral iron, Venofer or placebo

Correlates to the mortality data include a slightly higher rate of serious cardiac events among patients receiving Injectafer than oral iron (0.9% vs. 0.4% in oral-iron controlled studies) and the relatively common occurrence of grade 3 hypophosphatemia (8 to 70% vs. 0 in oral-iron controlled, PP and HUB studies).

Do the clinical data indicate that Injectafer is associated with a mortality disadvantage compared to oral iron? Please discuss your response.

2. Injectafer is proposed for use in the treatment of iron deficiency anemia in PP women or women who are anemic secondary to HUB. Injectafer has been shown to replenish iron and improve hemoglobin concentrations in these patients. Some women with anemia secondary to the PP condition or HUB can be successfully treated with oral iron. Clinical studies were not designed to assess the safety and efficacy of Injectafer specifically among women who had an unsatisfactory response to oral iron or were intolerant of oral iron. In addition, FDA has identified safety concerns of increased mortality and hypophosphatemia, as noted in question 1.

a. (Vote) Do the available efficacy and safety data support a favorable benefit-risk assessment for Injectafer in the treatment of iron deficiency anemia in PP women or women with HUB, without qualifiers or restrictions in this proposed usage?

b. (Vote) If you voted "no" in 2a, do the available efficacy and safety data support a favorable benefit-risk assessment for Injectafer in the treatment of iron deficiency anemia in PP women or women with HUB who have had an unsatisfactory response to oral iron or were intolerant of oral iron? As noted above, this population was not studied and safety issues identified in question 1 have not been examined in this population in a randomized trial in which Injectafer was compared to other parenteral iron compounds.

3. (Discussion) If you recommend marketing approval, please discuss designs for studies that FDA should request the manufacturer conduct post-marketing.

4. (Discussion) If you do not recommend marketing approval, discuss the important features of additional clinical studies to characterize safety and establish net clinical benefit for Injectafer.