IV. Question-Based Review

A. General Attributes

Ferrlecit is a macromolecular complex with an apparent molecular weight of 350,000 ± 23,000 D. The complex is formed by chelation of gluconate molecules to ferric ions.

Ferrlecit was approved for marketing in the US on 2/18/99 for treatment of iron deficiency anemia in patients undergoing chronic hemodialysis who are receiving supplemental epoetin therapy.

Each ampule of 5 ml Ferrlecit for I.V. injection contains 62.5 mg (12.5 mg/mL) of elemental iron as the sodium salt of a ferric ion carbohydrate complex in an alkaline aqueous solution with approximately 20% sucrose (w/v) in water for injection, pH 7.7-9.7. Each mL also contains 9 mg of benzyl alcohol as an inactive ingredient.

B. General Clinical Pharmacology

1. Do the findings of the PK study support the proposed dosage recommendations in pediatric patients aged 6-16 years?

Study FR01006 evaluated the comparative effectiveness and single dose PK profiles for two Ferrlecit doses in pediatric patients with iron deficiency undergoing chronic hemodialysis that were receiving supplemental erythropoietin therapy.

The study was a randomized, double-blind, multiple dose, parallel-group, multi-center study in pediatric hemodialysis (HD) patients (n = 66, age 12.1 ± 2.6 yrs, Wt 35.0 ± 16.6 kg). Patients determined to be iron-deficient[1] following suspension of their normal iron supplementation for 4 weeks (i.e., at Screening Visit 5), were randomized to a Ferrlecit dose of either 1.5 mg/kg (n = 22) or 3.0 mg/kg (n = 26), infused I.V. by syringe pump over 1 hour, not to exceed 125 mg per dose, during eight consecutive HD sessions over an approximate 22 day period. Blood samples were drawn for determination of Ferrlecit PK at 0 (pre-dose), 0.5, 1, 1.25, 1.5, 2, 3, 4, 6 and 48 hrs.

Table 1. Summary of the PK parameters following administration of 1.5 mg/kg and 3 mg/kg single doses of Ferrlecit to iron-deficient pediatric hemodialysis (HD) patients

Pharmacokinetic Parameter	1.5 mg/kg Ferrlecit® (n = 22)	3.0 mg/kg Ferrlecit® (n = 26)
C_{max} (mean ± SD μg/dL)	1287 ± 285	2283 ± 637
AUC_{0-48} (mean±SD μg•hr/dL)	9327 ± 4038	16,830 ± 6526
$AUC_{0-\infty}$ (mean ± SD μg•hr/dL)	9499 ± 4089	17,087 ± 6776
T_{max} (median hrs)	1.0	1.0
$t_{1/2}$ (median hrs)	2.0	2.1
K_{el} (mean ± SD hr-1)	0.43 ± 0.30	0.39 ± 0.27
Cl (mean ± SD L/hr)	0.69 ± 0.50	0.66 ± 0.52
V_d (mean ± SD L)	1.6 ± 0.6	1.9 ± 1.1

[1] Defined as having TSAT < 20% and/or serum ferritin < 100 ng/ml.

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