Injectafer treatment may be repeated if iron deficiency anemia reoccurs. Monitor serum phosphate levels in patients at risk for low serum phosphate who require a repeat course of treatment. Hypersensitivity reactions or signs and symptoms of hypersensitivity during and after Injectafer administration for at least 30 minutes and until clinically stable following completion of each administration. Monitor patients closely for signs and symptoms of hypertension following each Injectafer administration.

ADVERSE REACTIONS

The most common adverse reactions (≥2%) are nausea, hypertension, flushing, injection site reactions, erythema, hypophosphatemia, and dizziness. To report SUSPECTED ADVERSE REACTIONS, contact American Regent at 1-800-734-9236 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

USE IN SPECIFIC POPULATIONS

Pregnancy: Risk of hypersensitivity reactions which may have serious consequences for the fetus. See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

CONTRAINDICATIONS

Hypersensitivity to Injectafer or any of its inactive components. When added to an infusion bag containing 0.9% sodium chloride injection, USP, at concentrations ranging from 2 mg to 4 mg of iron per mL, Injectafer solution is physically and chemically stable for 72 hours when stored at room temperature. To maintain stability, do not dilute to concentrations less than 2 mg iron/mL.

To inspect parenteral drug products visually for the absence of particulate matter and discoloration prior to administration. The product contains no preservatives. Each vial of Injectafer is intended for single-dose only.

When administering Injectafer 750 mg as a slow intravenous push, give at the rate of approximately 100 mg (2 mL) per minute. For Injectafer 1000 mg, administer as a slow intravenous push over 15 minutes. Avoid extravasation of Injectafer since brown discoloration of the extravasation site may be long lasting. Monitor for extravasation. If extravasation occurs, discontinue the Injectafer administration at that site. Discard unused portion.

CONTRAINdications

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

INJECTAFER® (ferric carboxymaltose injection), for intravenous use

Dosage and Administration, Recommended Dosage

Recommended Dosage

For patients weighing 50 kg or more, the recommended dosage is Injectafer 750 mg intravenously in two doses separated by at least 7 days for a total cumulative dose of 1,500 mg of iron per course. Alternatively, for patients weighing 50 kg or more, Injectafer 15 mg/kg to a maximum of 1,000 mg may be administered as a single-dose treatment course.

For patients weighing less than 50 kg, the recommended dosage is Injectafer 15 mg/kg body weight intravenously in two doses separated by at least 7 days per course. For patients weighing 50 kg or more, Injectafer treatment may be repeated if iron deficiency anemia reoccurs.

Dosage Forms and Strengths

Injectafer solution is provided in single-dose vials containing concentrations ranging from 2 mg to 4 mg of iron per mL, Injectafer solution is physically and chemically stable for 72 hours when stored at room temperature. To maintain stability, do not dilute to concentrations less than 2 mg iron/mL.

Inspect parenteral drug products visually for the absence of particulate matter and discoloration prior to administration. The product contains no preservatives. Each vial of Injectafer is intended for single-dose only.

When added to an infusion bag containing 0.9% sodium chloride injection, USP, at concentrations ranging from 2 mg to 4 mg of iron per mL, Injectafer solution is physically and chemically stable for 72 hours when stored at room temperature. To maintain stability, do not dilute to concentrations less than 2 mg iron/mL.

Inspect parenteral drug products visually for the absence of particulate matter and discoloration prior to administration. The product contains no preservatives. Each vial of Injectafer is intended for single-dose only.

When administering Injectafer 750 mg as a slow intravenous push, give at the rate of approximately 100 mg (2 mL) per minute. For Injectafer 1000 mg, administer as a slow intravenous push over 15 minutes. Avoid extravasation of Injectafer since brown discoloration of the extravasation site may be long lasting. Monitor for extravasation. If extravasation occurs, discontinue the Injectafer administration at that site. Discard unused portion.

Repeat Treatment Monitoring Safety Assessment

Injectafer treatment may be repeated if IDA reoccurs. Monitor serum phosphate levels in patients at risk for low serum phosphate who require a repeat course of treatment.

Dosage Forms and Strengths

Injection: 50 mg/mL (3) • 750 mg iron/15 mL single-dose vial • 1,000 mg iron/20 mL single-dose vial.

Use in Specific Populations

Pregnancy: Risk of hypersensitivity reactions which may have serious consequences for the fetus. See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Recommended Dosage

Recommended Dosage

For patients weighing 50 kg or more, the recommended dosage is Injectafer 750 mg intravenously in two doses separated by at least 7 days for a total cumulative dose of 1,500 mg of iron per course. Alternatively, for patients weighing 50 kg or more, Injectafer 15 mg/kg to a maximum of 1,000 mg may be administered as a single-dose treatment course.

For patients weighing less than 50 kg, the recommended dosage is Injectafer 15 mg/kg body weight intravenously in two doses separated by at least 7 days per course. For patients weighing 50 kg or more, Injectafer treatment may be repeated if iron deficiency anemia reoccurs.

Dosage Forms and Strengths

Injectafer solution is provided in single-dose vials containing concentrations ranging from 2 mg to 4 mg of iron per mL, Injectafer solution is physically and chemically stable for 72 hours when stored at room temperature. To maintain stability, do not dilute to concentrations less than 2 mg iron/mL.

Inspect parenteral drug products visually for the absence of particulate matter and discoloration prior to administration. The product contains no preservatives. Each vial of Injectafer is intended for single-dose only.

When added to an infusion bag containing 0.9% sodium chloride injection, USP, at concentrations ranging from 2 mg to 4 mg of iron per mL, Injectafer solution is physically and chemically stable for 72 hours when stored at room temperature. To maintain stability, do not dilute to concentrations less than 2 mg iron/mL.

Inspect parenteral drug products visually for the absence of particulate matter and discoloration prior to administration. The product contains no preservatives. Each vial of Injectafer is intended for single-dose only.

When administering Injectafer 750 mg as a slow intravenous push, give at the rate of approximately 100 mg (2 mL) per minute. For Injectafer 1000 mg, administer as a slow intravenous push over 15 minutes. Avoid extravasation of Injectafer since brown discoloration of the extravasation site may be long lasting. Monitor for extravasation. If extravasation occurs, discontinue the Injectafer administration at that site. Discard unused portion.

Repeat Treatment Monitoring Safety Assessment

Injectafer treatment may be repeated if IDA reoccurs. Monitor serum phosphate levels in patients at risk for low serum phosphate who require a repeat course of treatment.

Dosage Forms and Strengths

Injection: 50 mg/mL, dark brown, non-transparent, sterile, aqueous solution. • 750 mg iron/15 mL single-dose vial • 1,000 mg iron/20 mL single-dose vial.

Contraindications

Injectafer is contraindicated in patients with a history of hypersensitivity to Injectafer or any of its components.
5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity Reactions

Serious hypersensitivity reactions, including anaphylactic-type reactions, some of which have been life-threatening and fatal, have been reported in patients receiving Injectafer. Patients may present with shock, clinically significant hypotension, loss of consciousness, and/or collapse. Monitor patients for signs and symptoms of hypersensitivity 15 minutes after completion of the infusion and at least 30 minutes and until clinically stable following completion of the infusion. Only administer Injectafer when personnel and therapies are immediately available for the treatment of serious hypersensitivity reactions. In clinical trials, serious anaphylactic/anaphylactoid reactions were reported in 0.1% (2/1,775) of subjects receiving Injectafer. Other serious or severe adverse reactions potentially associated with hypersensitivity which included, but not limited to, pruritus, rash, urticaria, wheezing, or hypotension were reported in 1.5% (26/1,775) of these subjects.

5.2 Symptomatic Hypophosphatemia

Symptomatic hypophosphatemia requiring clinical intervention has been reported in patients at risk of low serum phosphate in the postmarketing setting. These cases have developed mostly after repeat exposure to Injectafer in patients with a reported history of renal impairment. Possible risk factors for hypophosphatemia include a history of gastrointestinal disorders associated with malabsorption of fat-soluble vitamins or phosphate, concurrent or prior use of medications that affect proximal renal tubular function, hyperparathyroidism, vitamin D deficiency and malnutrition. In most cases, hypophosphatemia resolved within three months.

Monitor serum phosphate levels in patients at risk for low serum phosphate who require a repeat course of treatment.

5.3 Hypertension

In clinical studies, hypertension was reported in 4% (67/1,775) of subjects in clinical trials 1 and 2. Transient elevations in systolic blood pressure, sometimes occurring with facial flushing, dizziness, or nausea were observed in 6% (106/1,775) of subjects in these two clinical trials. These elevations generally occurred immediately after dosing and resolved within 30 minutes. Monitor patients for signs and symptoms of hypertension following each Injectafer administration.

5.4 Laboratory Test Alterations

In the 24 hours following administration of Injectafer, laboratory assays may overestimate serum iron and transferrin bound iron by also measuring the iron in Injectafer.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are discussed in greater detail in other sections of the labeling:

• Hypersensitivity Reactions
• Hypophosphatemia
• Hypertension
• Laboratory Test Alterations

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, the adverse reaction rates observed cannot be directly compared to rates in other clinical trials and may not reflect the rates observed in clinical practice.

In two randomized clinical studies, a total of 1,775 patients were exposed to Injectafer 15 mg/kg body weight up to a maximum single dose of 750 mg of iron on two occasions separated by at least 7 days up to a cumulative dose of 1,500 mg of iron.

Adverse reactions reported by ≥1% of treated patients are shown in the following table.

Table 1. Adverse reactions reported in ≥1% of Study Patients in Clinical Trials 1 and 2

<table>
<thead>
<tr>
<th></th>
<th>Injectafer (N=1,775) %</th>
<th>Pooled Comparatorsb (N=1,783) %</th>
<th>Oral iron (N=253) %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>7.2</td>
<td>2.2</td>
<td>1.2</td>
</tr>
<tr>
<td>Hypertension*</td>
<td>4.2</td>
<td>0.4</td>
<td></td>
</tr>
<tr>
<td>Flushing*</td>
<td>4.0</td>
<td>0.2</td>
<td></td>
</tr>
<tr>
<td>Injection site reactions*</td>
<td>3.2</td>
<td>0.6</td>
<td></td>
</tr>
<tr>
<td>Erythema</td>
<td>3.6</td>
<td>0.6</td>
<td></td>
</tr>
<tr>
<td>Hypophosphatemia</td>
<td>2.1</td>
<td>0.1</td>
<td></td>
</tr>
<tr>
<td>Dizziness*</td>
<td>2.1</td>
<td>1.3</td>
<td>0.4</td>
</tr>
<tr>
<td>Vomiting</td>
<td>2.1</td>
<td>1.2</td>
<td>0.4</td>
</tr>
<tr>
<td>Injection Site Discoloration**</td>
<td>1.4</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>Headache*</td>
<td>1.3</td>
<td>1.2</td>
<td>0.4</td>
</tr>
</tbody>
</table>

(ab) Included studies 1VIT07017, 1VIT07018, 1VIT09030 and 1VIT09031

*Grouped Terms
**Injection site discoloration and injection site discoloration were also included in the injection site reactions grouped term.

Table 2. Adverse Reactions (≥1% in any Treatment Group) in Patients Receiving a Single dose of Injectafer 15 mg/kg up to a Maximum of 1,000 mg or Two Doses of 15 mg/kg up to a Maximum of 750 mg to a Cumulative dose of 1,500 mg

<table>
<thead>
<tr>
<th></th>
<th>Injectafer 15 mg/kg to a maximum of 750 mg x 2 doses to a cumulative dose of 1,500 mg</th>
<th>Injectafer 15 mg/kg to a maximum of 1,000 mg single dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>(NCT00930) and (NCT00931)* (n=1,775)</td>
<td></td>
<td>(NCT00930) and (NCT00931)* (n=1,200)</td>
</tr>
<tr>
<td>Any Adverse Reaction</td>
<td>24</td>
<td>12</td>
</tr>
<tr>
<td>Injection site reactions*</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Injection site extravasation**</td>
<td>0.2</td>
<td>2</td>
</tr>
<tr>
<td>Hepatic enzyme increased*</td>
<td>1.2</td>
<td>1.2</td>
</tr>
<tr>
<td>Rash*</td>
<td>1.2</td>
<td>1.2</td>
</tr>
<tr>
<td>Headache*</td>
<td>1.3</td>
<td>1</td>
</tr>
<tr>
<td>Dizziness*</td>
<td>2.1</td>
<td>1</td>
</tr>
<tr>
<td>Dysgeusia*</td>
<td>1.2</td>
<td>1</td>
</tr>
<tr>
<td>Nausea</td>
<td>7.2</td>
<td>1</td>
</tr>
<tr>
<td>Hypertension*</td>
<td>4.1</td>
<td>1</td>
</tr>
<tr>
<td>Hypophosphatemia</td>
<td>2.1</td>
<td>1</td>
</tr>
<tr>
<td>Erythema*</td>
<td>3.6</td>
<td>0.3</td>
</tr>
<tr>
<td>Flushing*</td>
<td>4.3</td>
<td>0.3</td>
</tr>
<tr>
<td>Vomiting</td>
<td>2.1</td>
<td>0.2</td>
</tr>
<tr>
<td>Injection site discoloration**</td>
<td>1.4</td>
<td>&lt;0.1</td>
</tr>
<tr>
<td>Headache*</td>
<td>1.4</td>
<td>&lt;0.1</td>
</tr>
</tbody>
</table>

Other adverse reactions reported by ≥0.5% of treated patients include abdominal pain, diarrhea, gamma glutamyl transferase increased, parasthesia, and sneezing. Transient decreases in laboratory blood phosphorus levels (<2 mg/dL) have been observed in 27% (440/1,638) of patients in clinical trials.

Pooled data from two Phase 3 studies 1VIT09030 (NCT00981045) and 1VIT09031 (NCT00982007) with a dosing regimen of Injectafer 15 mg/kg up to a maximum of 750 mg x 2 doses to a cumulative dose of 1,500 mg of iron were analyzed to compare rates of adverse reactions in two Phase 3 parallel group studies 1 VIT07017 (NCT00548860) and 1 VIT07018 (NCT00548861) with a dosing regimen of Injectafer 15 mg/kg up to a maximum of 1,000 mg single dose (Table 2).
6.2 Post-marketing Experience
The following adverse reactions have been identified during post approval use of Injectafer. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

The following adverse reactions have been reported from the post-marketing spontaneous reports with Injectafer:
- Cardiac disorders: Tachycardia
- General disorders and administration site conditions: Chest discomfort, chills, pyrexia
- Metabolism and nutrition disorders: Hyperphosphatemia
- Musculoskeletal and connective tissue disorders: Arthralgia, back pain
- Nervous system disorders: Syncope
- Respiratory, thoracic and mediastinal disorders: Dyspnea
- Skin and subcutaneous tissue disorders: Angioedema, erythema, pruritus, urticaria
- Pregnancy: Fetal bradycardia

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary
Parenteral iron administration may be associated with hypersensitivity reactions [see Warnings and Precautions (5.1)], which may have serious consequences, such as fetal bradycardia [see Clinical Considerations]. Advise pregnant women of the potential risk to a fetus. Published studies and available data from postmarketing reports with intravenous Injectafer are insufficient to assess the risk of major birth defects and miscarriage.

There are risks to the mother and fetus associated with untreated IDA in pregnancy as well as to the fetus associated with maternal severe hypersensitivity reactions [see Clinical Considerations].

In animal reproduction studies, administration of ferric carboxymaltose to rabbits during the period of organogenesis caused adverse developmental outcomes including fetal malformations and increased implantation loss at maternally toxic doses of approximately 12% to 23% of the human weekly dose of 750 mg (based on body surface area).

The estimated risk of major birth defects and miscarriage for the indicated populations is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Clinical Considerations
Disease-associated maternal and/or embryo/fetal risk
Untreated IDA in pregnancy is associated with adverse maternal outcomes such as postpartum anemia. Adverse pregnancy outcomes associated with IDA include increased risk for preterm delivery and low birth weight.

Fetal/Neonatal adverse reactions
Severe adverse reactions including circulatory failure (severe hypotension, shock including in the context of anaphylactic reaction) may occur in pregnant women with parenthelial iron products (such as Injectafer) which may cause fetal bradycardia, especially during the second and third trimester.

Data
Human Data
Published data from randomized controlled studies, prospective observational studies and retrospective studies on the use of ferric carboxymaltose in pregnant women have not reported an association with intravenous ferric carboxymaltose and major birth defects and miscarriage. However, these studies cannot establish or exclude the absence of any drug-related risk during pregnancy.

Animal Data
Administration of ferric carboxymaltose to rats as a one-hour intravenous infusion up to 30 mg/kg/day of iron on gestation days 6 to 17 did not result in adverse embroyic or fetal findings. This daily dose in rats is approximately 40% of the human weekly dose of 750 mg based on body surface area. In rabbits, ferric carboxymaltose was administered as a one-hour infusion on gestation days 6 to 19 at iron doses of 4.5, 9, 13.5, and 18 mg/kg/day. Malformations were seen starting at the daily dose of 9 mg/kg (23% of the human weekly dose of 750 mg). Spontaneous abortions occurred starting at the daily dose of 4.5 mg/kg (12% of the human weekly dose of 750 mg based on body surface area). Pre-implantation loss was at the highest dose. Adverse embryonic or fetal effects were observed in the presence of maternal toxicity.

A pre- and post-natal development study was conducted in rats at intravenous doses up to 18 mg/kg/day of iron (approximately 25% of the weekly human dose of 750 mg based on body surface area). There were no adverse effects on survival of offspring, their behavior, sexual maturation or reproductive parameters.

8.2 Lactation

Risk Summary
The available published data on the use of ferric carboxymaltose in lactating women demonstrate that iron is present in breast milk. Among the breastfed infants, adverse reactions included constipation and diarrhea but none of the adverse reactions reported were considered related to ferric carboxymaltose exposure through breastmilk. There is no information on the effects of ferric carboxymaltose on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for Injectafer in addition to any potential adverse effects on the breastfed child from the drug or from the underlying maternal condition.

8.4 Pediatric Use
Safety and effectiveness have not been established in pediatric patients.

8.5 Geriatric Use
Of the 1,775 subjects in clinical studies of Injectafer, 50% were 65 years and over, while 25% were 75 years and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

10 OVERDOSAGE
Excessive dosages of Injectafer may lead to accumulation of iron in storage sites potentially leading to hemosiderosis. A patient who received Injectafer 18,000 mg over 6 months developed hemosiderosis with multiple joint disorder, walking disability, and anemia. Hypophosphatemic osteomalacia was reported in a patient who received Injectafer 4,000 mg over 4 months. Partial recovery followed discontinuation of Injectafer.

11 DESCRIPTION
Ferric carboxymaltose, an iron replacement product, is an iron carbohydrate complex with the chemical name of polymeric iron (III) hydroxide 4(R)-poly([1→4]-D-glucopyranosyl)-oxy-2(R),3(S),5(R),6-tetrahydroxy-hexanoate. It has a relative molecular weight of approximately 150,000 Da corresponding to the following empirical formula: \[\text{FeO}_5\text{(OH)}_5\text{H}_2\text{O}]\_m \{[(\text{C}_6\text{H}_{10}\text{O}_5)_m (\text{C}_6\text{H}_{12}\text{O}_7)\}_k\}x\]
where \(n \approx 10^3, m \approx 8, k = 11, \) and \(x\) represents the mean branching degree of the ligand.

The chemical structure is presented below:

Injectafer (ferric carboxymaltose injection) is a dark brown, sterile, aqueous, isotonic, nonpyrogenic, nonendotoxin solution containing 100 mg of ferric carboxymaltose per mL.

Vial closure is not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
Ferric carboxymaltose is a colloidal iron (III) hydroxide in complex with carboxymaltose, a carbohydrate polymer that releases iron.

12.2 Pharmacodynamics
Using positron emission tomography (PET) it was demonstrated that red cell uptake of \(^{59}\text{Fe}\) and \(^{59}\text{Fe}\) from Injectafer ranged from 61% to 99%. In patients with iron deficiency, red cell uptake of radiolabeled iron ranged from 91% to 99% at 24 days after Injectafer dose. In patients with renal anemia, red cell uptake of radiolabeled iron ranged from 61% to 84% at 24 days after Injectafer dose.

12.3 Pharmacokinetics
After administration of a single dose of Injectafer of 100 to 1,000 mg of iron in iron deficient patients, maximum iron concentration of 37 μg/mL to 333 μg/mL were obtained respectively after 15 minutes to 1.21 hours post dose. The volume of distribution was estimated to be 3 L.

The iron injected or infused was rapidly cleared from the plasma, the terminal half-life ranging from 7 to 12 hours. Renal elimination of iron was negligible.

13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
Carcinogenicity studies have not been performed with ferric carboxymaltose.

Ferric carboxymaltose was not genotoxic in the following genetic toxicity studies: in vitro microbial mutagenesis (Ames) assay, in vitro chromosome aberration test in human lymphocytes, in vitro mammalian cell mutation assay in mouse lymphoma L5178Y/TK-/- cells, in vivo mouse micronucleus test at single intravenous doses up to 500 mg/kg.

In a combined male and female fertility study, ferric carboxymaltose was administered intravenously over one hour to male and female rats at iron doses of up to 30 mg/kg. Animals were dosed 3 times per week (on Days 3, 0, and 7). There was no effect on mating function, fertility or early embryonic development. Based on body...
14 CLINICAL STUDIES
The safety and efficacy of Injectafer for treatment of IDA were evaluated in two randomized, open-label, controlled clinical trials (Trial 1 and Trial 2). In these two trials, Injectafer was administered at a dose of 15 mg/kg body weight up to a maximum single dose of 750 mg of iron on two occasions separated by at least 7 days up to a cumulative dose of 1,500 mg of iron.

14.1 Trial 1: Iron Deficiency Anemia in Patients Who Are Intolerant to Oral Iron or Have Had Unsatisfactory Response to Oral Iron
Trial 1: A Multi-center, Randomized, Active Controlled Study to Investigate the Efficacy and Safety of Intravenous Ferric Carboxymaltose (FCM) in Patients with Iron Deficiency Anemia (IDA), (NCT00982007) was a randomized, open-label, controlled clinical study in patients with IDA who had an unsatisfactory response to oral iron (Cohort 1) or who were intolerant to oral iron (Cohort 2) during the 14-day oral iron run-in period. Inclusion criteria prior to randomization included hemoglobin (Hb) <12 g/dL, ferritin ≤100 ng/mL or ferritin ≤300 ng/mL when transferrin saturation (TSAT) ≤30%. Cohort 1 subjects were randomized to Injectafer or oral iron for 14 more days. Cohort 2 subjects were randomized to Injectafer or another IV iron per standard of care (90% of subjects received iron sucrose). The mean age of study patients was 43 years (range, 18 to 94); 94% were female; 42% were Caucasian, 32% were African American, 24% were Hispanic, and 2% were other races.

Table 3 shows the baseline and the change in hemoglobin from baseline to highest value between baseline and Day 56 or time of intervention.

Table 3. Mean Change in Hemoglobin From Baseline to the Highest Value Between Day 35 or Time of Intervention (Modified Intent-to-Treat Population)

<table>
<thead>
<tr>
<th>Hemoglobin (g/dL)</th>
<th>Cohort 1 (N=244)</th>
<th>Cohort 2 (N=251)</th>
<th>IV SCa (N=237)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>10.6 (1.0)</td>
<td>10.6 (1.0)</td>
<td>9.1 (1.6)</td>
</tr>
<tr>
<td>Highest Value</td>
<td>12.2 (1.1)</td>
<td>11.4 (1.2)</td>
<td>12.0 (1.2)</td>
</tr>
<tr>
<td>Change (from baseline to highest value)</td>
<td>1.6 (1.2)</td>
<td>0.8 (0.8)</td>
<td>2.9 (1.6)</td>
</tr>
<tr>
<td>p-value</td>
<td>0.001</td>
<td>0.001</td>
<td>0.001</td>
</tr>
</tbody>
</table>

SD=standard deviation; a: Intravenous iron per standard of care

Increases from baseline in mean ferritin (264.2 ± 224.2 mg/dL in Cohort 1 and 218.2 ± 211.4 mg/dL in Cohort 2), and transferrin saturation (13 ± 16% in Cohort 1 and 20 ± 15% in Cohort 2) were observed at Day 35 in Injectafer-treated patients.

14.2 Trial 2: Iron Deficiency Anemia in Patients with Non-Dialysis Dependent Chronic Kidney Disease
Trial 2: REPAIR-IDA, Randomized Evaluation of efficacy and safety of Ferric Carboxymaltose in Patients with Iron Deficiency Anemia and Impaired Renal function, (NCT00981045) was a randomized, open-label, controlled clinical study in patients with non-dialysis dependent chronic kidney disease. Inclusion criteria included hemoglobin (Hb) ≤11.5 g/dL, ferritin ≤100 ng/mL or ferritin ≤300 ng/mL when transferrin saturation (TSAT) ≤30%. Study patients were randomized to either Injectafer or Venofer. The mean age of study patients was 67 years (range, 19 to 101); 64% were female; 54% were Caucasian, 26% were African American, 18% Hispanics, and 2% were other races.

Table 4 shows the baseline and the change in hemoglobin from baseline to highest value between baseline and Day 56 or time of intervention.

Table 4. Mean Change in Hemoglobin From Baseline to the Highest Value Between Baseline and Day 56 or Time of Intervention (Modified Intent-to-Treat Population)

<table>
<thead>
<tr>
<th>Hemoglobin (g/dL)</th>
<th>Injectafer (N=1,249)</th>
<th>Venofer (N=1,244)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>10.3 (0.8)</td>
<td>10.3 (0.8)</td>
</tr>
<tr>
<td>Highest Value</td>
<td>11.4 (1.2)</td>
<td>11.3 (1.1)</td>
</tr>
<tr>
<td>Change (from baseline to highest value)</td>
<td>1.1 (1.0)</td>
<td>0.9 (0.92)</td>
</tr>
<tr>
<td>Treatment Difference (95% CI)</td>
<td>0.21 (0.13, 0.28)</td>
<td></td>
</tr>
</tbody>
</table>

Increases from baseline in mean ferritin (734.7 ± 337.8 ng/mL), and transferrin saturation (30 ± 17%) were observed prior to Day 56 in Injectafer-treated patients.

16 HOW SUPPLIED/STORAGE AND HANDLING
Injectafer (ferric carboxymaltose injection) is a dark brown, non-transparent, sterile, aqueous solution.

NDC 0517-0650-01 750 mg iron/15 mL Single-Dose Vial Individually Boxed
NDC 0517-0620-01 1,000 mg iron/20 mL Single-Dose Vial Individually Boxed

Store at 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F). [See the USP controlled room temperature.] Do not freeze.

American Regent, Inc.
Shirley, NY 11967

Injectafer is manufactured under license from Vifor (International) Inc, Switzerland.
What is INJECTAFER?
INJECTAFER is a prescription iron replacement medicine used to treat IDA in adults who have:

• intolerance to oral iron or who have not responded well to treatment with oral iron, or

• non-dialysis dependent chronic kidney disease

It is not known if INJECTAFER is safe and effective for use in children.

Who should not receive INJECTAFER?
Do not receive INJECTAFER if you are allergic to ferric carboxymaltose or any of the ingredients in INJECTAFER. See the end of this leaflet for a complete list of ingredients in INJECTAFER.

Before receiving INJECTAFER, tell your healthcare provider about all of your medical conditions, including if you:

• have had an allergic reaction to iron given into your vein

• have high blood pressure

• are pregnant or plan to become pregnant. It is not known if INJECTAFER will harm your unborn baby.

• are breastfeeding or plan to breastfeed. INJECTAFER passes into your breast milk. It is unknown whether INJECTAFER would pose a risk to your baby. Talk to your healthcare provider about the best way to feed your baby during treatment with INJECTAFER.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How will I receive INJECTAFER?
INJECTAFER is given intravenously (into your vein) by your healthcare provider in 2 doses at least 7 days apart or given as a single dose.

What are the possible side effects of INJECTAFER?
INJECTAFER may cause serious side effects, including:

• Allergic (hypersensitivity) reactions. Serious life-threatening allergic reactions have happened in people who receive INJECTAFER. Other serious reactions including itching, hives, wheezing, and low blood pressure also have happened during treatment with INJECTAFER. Tell your healthcare provider if you have ever had any unusual or allergic reaction to any iron given by vein.

• High blood pressure (hypertension). High blood pressure, sometimes with face flushing, dizziness, or nausea, has happened during treatment with INJECTAFER. Your healthcare provider will check your blood pressure and check for any signs and symptoms of high blood pressure after you receive INJECTAFER.

The most common side effects of INJECTAFER include:

• nausea
• dizziness
• flushing
• low levels of phosphorous in your blood
• high blood pressure

These are not all the possible side effects of INJECTAFER.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about INJECTAFER
Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. You can ask your pharmacist or healthcare provider for information about INJECTAFER that is written for health professionals.

What are the ingredients in INJECTAFER?
Active ingredient: ferric carboxymaltose

Inactive ingredients: water for injection. Sodium hydroxide and/or hydrochloric acid may have been added to adjust pH to 5.0-7.0.

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For more information go to www.injectafer.com or call 1-800-734-9236.

This Patient Information has been approved by the U.S. Food and Drug Administration.
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