

## HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Injactafer safely and effectively. See full prescribing information for Injactafer.

**INJECTAFER® (ferric carboxymaltose injection), for intravenous use Initial U.S. Approval: 2013**

### RECENT MAJOR CHANGES

Indications and Usage. (1) 11/2021  
Dosage and Administration, Recommended Dosage. (2.1) 04/2021

### INDICATIONS AND USAGE

Injactafer is an iron replacement product indicated for the treatment of iron deficiency anemia (IDA) in:

- Adults and pediatric patients 1 year of age and older who have either intolerance to oral iron or an unsatisfactory response to oral iron. (1)
- Adult patients who have non-dialysis dependent chronic kidney disease. (1)

### DOSAGE AND ADMINISTRATION

For patients weighing 50 kg or more, the recommended dosage is Injactafer 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. For adult patients weighing 50 kg or more, an alternative dose of Injactafer 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 Injactafer 15 mg/kg body weight intravenously in two doses separated by at least 7 days per course.

Injactafer treatment may be repeated if IDA reoccurs. (2)

### DOSAGE FORMS AND STRENGTHS

- Injection: 50 mg/mL (3)
- 100 mg iron/2 mL single-dose vial
  - 750 mg iron/15 mL single-dose vial
  - 1,000 mg iron/20 mL single-dose vial

## FULL PRESCRIBING INFORMATION: CONTENTS\*

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## FULL PRESCRIBING INFORMATION

### 1 INDICATIONS AND USAGE

Injactafer is indicated for the treatment of iron deficiency anemia (IDA) in:

- Adults and pediatric patients 1 year of age and older who have either intolerance to oral iron or an unsatisfactory response to oral iron.
- Adult patients who have non-dialysis dependent chronic kidney disease.

### 2 DOSAGE AND ADMINISTRATION

#### 2.1 Recommended Dosage

For patients weighing 50 kg or more, the recommended dosage is Injactafer 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. For adult patients weighing 50 kg or more, an alternative dose of Injactafer 15 mg/kg body weight up to a maximum of 1,000 mg intravenously may be administered as a single-dose treatment course.

For patients weighing less than 50 kg, the recommended dosage is Injactafer 15 mg/kg body weight intravenously in two doses separated by at least 7 days per course.

Each mL of Injactafer contains 50 mg of elemental iron.

#### 2.2 Preparation and Administration

Administer Injactafer intravenously, either as an undiluted slow intravenous push or by infusion. When administered via infusion, dilute up to 1,000 mg of iron in no more than 250 mL of sterile 0.9% sodium chloride injection, USP, such that the concentration of the infusion is not less than 2 mg of iron per mL and administer over at least 15 minutes.

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, Injactafer 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 Injactafer is intended for single-dose only.

When administering Injactafer 750 mg as a slow intravenous push, give at the rate of approximately 100 mg (2 mL) per minute. For Injactafer 1,000 mg, administer as a slow intravenous push over 15 minutes. Avoid extravasation of Injactafer since brown discoloration of the extravasation site may be long lasting. Monitor for extravasation. If extravasation occurs, discontinue the Injactafer administration at that site.

Discard unused portion.

#### 2.3 Repeat Treatment Monitoring Safety Assessment

Injactafer 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 [see Warnings and Precautions (5.2)].

## CONTRAINDICATIONS

Hypersensitivity to Injactafer or any of its inactive components. (4)

## WARNINGS AND PRECAUTIONS

- Hypersensitivity Reactions:** Observe for signs and symptoms of hypersensitivity during and after Injactafer administration for at least 30 minutes and until clinically stable following completion of each administration. (5.1)
- Symptomatic Hypophosphatemia:** Monitor serum phosphate levels in patients at risk for low serum phosphate who require a repeat course of treatment. (5.2)
- Hypertension:** Monitor patients closely for signs and symptoms of hypertension following each Injactafer administration. (5.3)

## ADVERSE REACTIONS

The most common adverse reactions (>2%) are nausea, hypertension, flushing, injection site reactions, erythema, hypophosphatemia, and dizziness. (6.1)

The most common adverse reactions in pediatric patients (≥4%) are hypophosphatemia, injection site reactions, rash, headache, and vomiting. (6.1)

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](http://www.fda.gov/medwatch).

## USE IN SPECIFIC POPULATIONS

Pregnancy: Risk of hypersensitivity reactions which may have serious consequences for the fetus. (8.1)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 02/2022

## 6 ADVERSE REACTIONS

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

- Hypersensitivity Reactions [see Warnings and Precautions (5.1)]
- Hypophosphatemia [see Warnings and Precautions (5.2)]
- Hypertension [see Warnings and Precautions (5.3)]
- Laboratory Test Alterations [see Warnings and Precautions (5.4)]

### 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.

#### Adults

In two randomized clinical studies [Studies 1 and 2, see Clinical Studies (14)], a total of 1,775 patients were exposed to Injactafer 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

	Injactafer (N=1,775) %	Pooled Comparators* (N=1,783) %	Oral iron (N=253) %
Nausea	7.2	2	1.2
Hypertension*	4	2	0.4
Flushing*	4	0.2	0
Injection site reactions*	3	3.2	0
Erythema*	3	0.6	0
Hypophosphatemia	2.1	0.1	0
Dizziness*	2.1	1.3	0.4
Vomiting	2	1	0.4
Injection Site Discoloration**	1.4	0.3	0
Headache*	1.3	1.2	0.4
Hepatic enzyme increased*	1.2	0.2	0
Dysgeusia*	1.2	2.1	0
Hypotension	1	2	0
Rash*	1	0.3	0
Constipation	0.5	0.9	3.2

\*Includes oral iron and all formulations of IV iron other than Injactafer

\*\*Grouped Terms:

Hypertension includes hypertension, blood pressure increased, and hypertensive crisis.

Flushing includes flushing and hot flush.

Injection site reactions include injection site extravasation, injection site discoloration, injection site pain, injection site irritation, injection site bruising, injection site reaction, injection site discomfort, injection site erythema, injection site hematoma, injection site hemorrhage, injection site pruritus, injection site rash, and injection site swelling.

Erythema includes erythema and injection site erythema.

Dizziness includes dizziness, balance disorder, and vertigo.

\*\* Injection site discoloration was also included in the injection site local administration reactions grouped term.

Headache includes headache and migraine.

Hepatic enzyme increased includes alanine aminotransferase increased and aspartate aminotransferase increased.

Dysgeusia includes dysgeusia and ageusia.

Rash includes rash, urticaria, skin exfoliation, blister, erythema multiforme, injection site rash, rash maculo-papular, and rash pruritic.

Other adverse reactions reported by ≥0.5% of treated patients include abdominal pain, diarrhea, gamma glutamyl transferase increased, paresthesia, 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 Injactafer 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 1VIT07017 (NCT00548860) and 1VIT07018 (NCT00548691) with a dosing regimen of Injactafer 15 mg/kg up to a maximum of 1,000 mg single dose (Table 2).

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

	Injactafer 15 mg/kg to a maximum of 750 mg x 2 doses to a cumulative dose of 1,500 mg	Injactafer 15 mg/kg to a maximum of 1,000 mg single dose
	1VIT09030 and 1VIT09031* (n=1,775) %	1VIT07017 and 1VIT07018*(n=1,200) %
Any Adverse Reaction	24	12
Injection site reactions*	3	4
Injection site extravasation**	0.2	2
Hepatic enzyme increased*	1.2	1.2
Rash*	1	1.2
Headache*	1.3	1
Dizziness*	2.1	1
Dysgeusia*	1.2	1
Nausea	7.2	1
Hypertension*	4	1
Hypophosphatemia	2.1	1
Erythema*	3	0.3
Flushing*	4	0.3
Vomiting	2	0.2
Injection site discoloration**	1.4	<0.1
Hypotension	1	<0.1

\*Included studies 1VIT07017, 1VIT07018, 1VIT09030 and 1VIT09031

\*\*Grouped Terms

\*\*Injection site extravasation and injection site discoloration were also included in the injection site reactions grouped term.

## Patient Information

### INJECTAFER (in-jekt-a-fer)

#### (ferric carboxymaltose injection)

### What is INJECTAFER?

INJECTAFER is a prescription iron replacement medicine used to treat iron deficiency anemia (IDA) in:

- Adults and pediatric patients 1 year of age and older who have either intolerance to oral iron or an unsatisfactory response to oral iron.
- Adult patients who have non-dialysis dependent chronic kidney disease

Safety and effectiveness of Injactafer have not been established in pediatric patients with IDA who are less than 1 year of age.

### 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.
- If your healthcare provider decides it is right for you, INJECTAFER may be given intravenously to adults by your healthcare provider as a single dose treatment.

### 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
- flushing
- skin redness (erythema)
- rash
- vomiting
- high blood pressure
- injection site reactions
- low levels of phosphorous in your blood
- headache

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.

(ferric carboxymaltose injection)

INJECTAFER®



RQ1052G

## 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.



For more information go to [www.injectafer.com](http://www.injectafer.com) or call 1-800-734-9236.

This Patient Information has been approved by the U.S. Food and Drug Administration. Revised: 02/2022

*Pediatric Patients*

The safety of Injectafer in pediatric patients was evaluated in study 1VIT17044 (NCT03523117; Study 3). Study 1VIT17044 was a randomized, active-controlled study in which 40 patients (1 to 12 years of age; 10 patients, 12 to 17 years of age; 30 patients) received Injectafer 15 mg/kg to a maximum single dose of 750 mg (whichever was smaller) on Days 0 and 7 for a maximum total dose of 1,500 mg; 38 patients evaluable for safety in the population of patients receiving formulation of oral ferrous sulfate for 28 days. The median age of patients who received Injectafer was 14.5 years (range, 1-17); 83% were female; 88% White and 13% Black. The most common adverse reactions (≥4%) were hypophosphatemia, injection site reactions, rash, headache, and vomiting.

Table 3 summarizes the adverse reactions in Study 3.

	<b>Injectafer (n=40) %</b>	<b>Oral Ferrous Sulfate (n=38) %</b>
Any Adverse Reactions	35	26
Hypophosphatemia*	13	0
Injection site reactions*	8	0
Rash*	8	0
Headache	5	3
Vomiting	5	3
Nasopharyngitis	3	5
Flushing	3	0
Gastrointestinal infections	3	0
Liver function test increased	3	0
Platelet count decreased	3	0
White blood cell count decreased	3	0

\*Grouped Terms

Injection site reactions include infusion site hematoma, infusion site hypoesthesia and injection site pain. Hypophosphatemia includes hypophosphatemia and blood phosphorus decreased. Rash includes rash, exanthema and urticaria.

### 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: Hypophosphatemia
- Musculoskeletal and connective tissue disorders: Arthralgia, back pain, hypophosphatemic osteomalacia (rarely reported event)
- 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 risks 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 background 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 post-partum 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 parenteral 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 iron on gestation days 6 to 17 did not result in adverse embryonic 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 iron 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 23% 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 include 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

The safety and effectiveness of Injectafer for IDA in pediatric patients aged 1 year and older who have normal kidney function and have either intolerance to oral iron or have had unsatisfactory response to oral iron have been established. Use of Injectafer for this indication in this age group is supported by evidence from adequate and well-controlled studies of Injectafer in adults with additional pharmacodynamic and safety data in pediatric patients aged 1 year and older *[see Adverse Reactions (6.1) and Clinical Pharmacology (12.3)]*.

Safety and effectiveness of Injectafer have not been established in pediatric patients less than 1 year of age with IDA.

## 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 asthenia. Hypophosphatemic osteomalacia was reported in a patient who received Injectafer 4,000 mg over 4 months. Partial recovery followed discontinuation of Injectafer.

## 11 DESCRIPTION

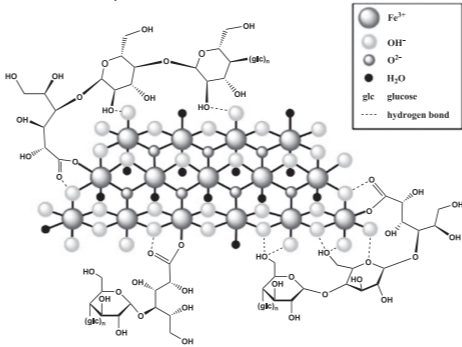
Ferric carboxymaltose, an iron replacement product, is an iron carbohydrate complex with the chemical name of polynuclear iron (III)-hydroxide 4(R)-(poly-(1→4)-*O*- $\alpha$ -D-glucopyranosyl)-oxy-2(R),3(R),5(R),6-tetrahydroxy-hexanoate. It has a relative molecular weight of approximately 150,000 Da corresponding to the following empirical formula:

$[FeO(OH)(H_2O)_n \{ (C_6H_{10}O_5)_m (C_6H_7O_5)_k \}]_x$ ,

where  $n \approx 10^3$ ;  $m \approx 8$ ;  $k \approx 11$ ; and  $k \approx 4$

(*k* 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 colloidal solution for intravenous injection. Each mL contains 50 mg iron as ferric carboxymaltose in water for injection. Injectafer is available in 2 mL, 15 mL and 20 mL single-dose vials. Sodium hydrochloric acid and/or hydrochloric acid may have been added to adjust the pH to 5.0-7.0.

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 <sup>59</sup>Fe and <sup>55</sup>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 adult 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 ranged from 7 to 12 hours. Renal elimination of iron was negligible.

After administration of a single dose of Injectafer 15 mg/kg in pediatric patients 1-17 years of age, the maximum concentrations ranged between 124 and 418.1 µg/mL and the median time to maximum concentration was 7 minutes. The elimination half-life of Injectafer in pediatric patients was approximately 9.7 hours. The total median 72-hour exposure (AUC<sub>0-72h</sub>) after a single dose of Injectafer 15 mg/kg in pediatric patients was 4529.7 µg·h/mL while the median exposure after a single dose of 1000 mg in adults was 5875.3 µg·h/mL.

## 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 toxicology 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 0, 3, and 7). There was no effect on mating function, fertility or early embryonic development. Based on body surface area, the dose of 30 mg/kg in animals is approximately 40% of the human dose of 750 mg.

## 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. The primary etiologies of IDA were heavy uterine bleeding (47%) and gastrointestinal disorders (17%).

Table 4 shows the baseline and the change in hemoglobin from baseline to highest value between baseline and Day 35 or time of intervention.

**Table 4. Mean Change in Hemoglobin From Baseline to the Highest Value Between Day 35 or Time of Intervention (Modified Intent-to-Treat Population)**

Hemoglobin (g/dL) Mean (SD)	Cohort 1		Cohort 2	
	Injectafer (N=244)	Oral Iron (N=251)	Injectafer (N=245)	IV SC <sup>a</sup> (N=237)
Baseline	10.6 (1.0)	10.6 (1.0)	9.1 (1.6)	9.0 (1.5)
Highest Value	12.2 (1.1)	11.4 (1.2)	12.0 (1.2)	11.2 (1.3)
Change (from baseline to highest value)	1.6 (1.2)	0.8 (0.8)	2.9 (1.6)	2.2 (1.3)
p-value	0.001		0.001	

SD=standard deviation; <sup>a</sup>: Intravenous iron per standard of care

Increases from baseline in mean ferritin (264.2 ± 224.2 ng/mL in Cohort 1 and 218.2 ± 211.4 ng/mL 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 5 shows the baseline and the change in hemoglobin from baseline to highest value between baseline and Day 56 or time of intervention.

**Table 5. Mean Change in Hemoglobin From Baseline to the Highest Value Between Baseline and Day 56 or Time of Intervention (Modified Intent-to-Treat Population)**

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

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 0517-0602-01	100 mg iron/2 mL Single-Dose Vial	Individually Boxed
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.

## 17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information) and discuss with the patient the etiology of the iron deficiency anemia and the patient's iron deficiency anemia treatment options.

#### *Prior History of Reactions to Parenteral Iron Products*

Question patients regarding any prior history of reactions to parenteral iron products *[see Warnings and Precautions (5.1)]*.

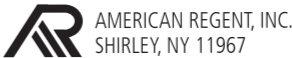
#### *Serious Hypersensitivity Reactions*

Advise patients to report any signs and symptoms of hypersensitivity that may develop during and following Injectafer administration, such as rash, itching, dizziness, lightheadedness, swelling, and breathing problems *[see Warnings and Precautions (5.1)]*.

#### *Pregnancy*

Advise pregnant women about the risk of hypersensitivity reactions which may have serious consequences for the fetus. Advise patients who may become pregnant to inform their healthcare provider of a known or suspected pregnancy *[see Use in Specific Populations (8.1)]*.

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