**HIGHLIGHTS OF PRESCRIBING INFORMATION**

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

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

**----------INDICATIONS AND USAGE----------**

Injectafer is an iron replacement product 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.

**----------DOSAGE AND ADMINISTRATION----------**

For patients weighing 50 kg (110 lb) or more: Give Injectafer in two doses separated by at least 7 days. Give each dose as 750 mg for a total cumulative dose of 1500 mg of iron per course.

For patients weighing less than 50 kg (110 lb): Give Injectafer in two doses separated by at least 7 days and give each dose as 15 mg/kg body weight.

Injectafer treatment may be repeated if iron deficiency anemia reoccurs. (2)

**----------DOSAGE FORMS AND STRENGTHS----------**

Injection: 750 mg iron / 15 mL single-dose vial. (3)

**----------CONTRAINDICATIONS----------**

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

**----------WARNINGS AND PRECAUTIONS----------**

- **Hypersensitivity reactions:** Observe for signs and symptoms of hypersensitivity during and after Injectafer administration for at least 30 minutes and until clinically stable following completion of each administration. (5.1)
- **Hypertension:** Monitor patients closely for signs and symptoms of hypertension following each Injectafer administration. (5.2)

**----------ADVERSE REACTIONS----------**

The most common adverse reactions (≥2%) are nausea, hypertension, flushing, hypophosphatemia, and dizziness. (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.***

**----------USE IN SPECIFIC POPULATIONS----------**

Lactation: Monitor breastfed infants for gastrointestinal toxicity. (8.2)

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

**Revised: 04/2018**

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**FULL PRESCRIBING INFORMATION: CONTENTS***



* Sections or subsections omitted from the full prescribing information are not listed.

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## FULL PRESCRIBING INFORMATION

## 1 INDICATIONS AND USAGE

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.

## 2 DOSAGE AND ADMINISTRATION

For patients weighing 50 kg (110 lb) or more: Give Injectafer in two doses separated by at least 7 days. Give each dose as 750 mg for a total cumulative dose not to exceed 1500 mg of iron per course.

For patients weighing less than 50 kg (110 lb): Give Injectafer in two doses separated by at least 7 days. Give each dose as 15 mg/kg body weight for a total cumulative dose not to exceed 1500 mg of iron per course.

The dosage of Injectafer is expressed in mg of elemental iron. Each mL of Injectafer contains 50 mg of elemental iron. Injectafer treatment may be repeated if iron deficiency anemia reoccurs.

Administer Injectafer intravenously, either as an undiluted slow intravenous push or by infusion. When administering as a slow intravenous push, give at the rate of approximately 100 mg (2 mL) per minute. When administered via infusion, dilute up to 750 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, 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. Any unused drug remaining after injection must be discarded.

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.

## 3 DOSAGE FORMS AND STRENGTHS

Injection: 750 mg iron / 15 mL single-dose vial

## 4 CONTRAINDICATIONS

Hypersensitivity to Injectafer or any of its components [see *Warnings and Precautions* (5.1)]

## 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 during and after Injectafer administration for 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. *[see Adverse Reactions (6.1, 6.2)]*. In clinical trials, serious anaphylactic/anaphylactoid reactions were reported in 0.1% (2/1775) 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% (26/1775) of these subjects.

### 5.2 Hypertension

In clinical studies, hypertension was reported in 3.8% (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 [*see Dosage and Administration (2)*].

### 5.3 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 adverse reactions are discussed in greater detail in other sections of the labeling:

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

### 6.1 Adverse Reactions in Clinical Trials

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 [Studies 1 and 2, *see Clinical Studies (14)*], 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 1500 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**

| Term | Injectafer (N=1775) % | Pooled Comparators[a] (N=1783) % | Oral iron (N=253) % |
|---|---|---|---|
| Nausea | 7.2 | 1.8 | 1.2 |
| Hypertension | 3.8 | 1.9 | 0.4 |
| Flushing/Hot Flush | 3.6 | 0.2 | 0.0 |
| Blood Phosphorus Decrease | 2.1 | 0.1 | 0.0 |
| Dizziness | 2.0 | 1.2 | 0.0 |
| Vomiting | 1.7 | 0.5 | 0.4 |
| Injection Site Discoloration | 1.4 | 0.3 | 0.0 |
| Headache | 1.2 | 0.9 | 0.0 |
| Alanine Aminotransferase Increase | 1.1 | 0.2 | 0.0 |
| Dysgeusia | 1.1 | 2.1 | 0.0 |
| Hypotension | 1.0 | 1.9 | 0.0 |
| Constipation | 0.5 | 0.9 | 3.2 |

[a] Includes oral iron and all formulations of IV iron other than Injectafer

Other adverse reactions reported by ≥ 0.5% of treated patients include abdominal pain, diarrhea, gamma glutamyl transferase increased, injection site pain/irritation, rash, paraesthesia, sneezing. Transient decreases in laboratory blood phosphorus levels (< 2 mg/dL) have been observed in 27% (440/1638) patients in clinical trials.

### 6.2 Post-marketing Experience

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 serious adverse reactions have been most commonly reported from the post-marketing spontaneous reports with Injectafer: urticaria, dyspnea, pruritus, tachycardia, erythema, pyrexia, chest discomfort, chills, angioedema, back pain, arthralgia, and syncope. One case of hypophosphatemic osteomalacia was reported in a subject who received 500 mg of Injectafer every 2 weeks for a total of 16 weeks. Partial recovery followed discontinuation of Injectafer.

## 8 USE IN SPECIFIC POPULATIONS

### 8.1 Pregnancy

*Risk Summary*

Published studies on the use of ferric carboxymaltose in pregnant women have not reported an association with ferric carboxymaltose and adverse developmental outcomes. However, these studies cannot establish or exclude the absence of any drug-related risk during pregnancy because the studies were not designed to assess for the risk of major birth defects (*see Data*). There are risks to the mother and fetus associated with untreated iron deficiency anemia (IDA) in pregnancy (*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. Adverse outcomes in pregnancy occur regardless of the health of the mother or the use of medications. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

*Clinical Considerations*

*Disease-Associated Maternal and/or Embryo/Fetal Risk*

Untreated iron deficiency anemia (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.

*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 ferric carboxymaltose and adverse developmental outcomes. However, these studies cannot establish or exclude the absence of any drug-related risk during pregnancy because of methodological limitations, including that the studies were not primarily designed to capture safety data nor designed to assess the risk of major birth defects. Maternal adverse events reported in these studies are similar to those reported during clinical trials in adult males and non-pregnant females *[see Adverse Reactions (6.1)]*.

*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 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 on a body surface area basis). There were no adverse effects on survival of offspring, their behavior, sexual maturation or reproductive parameters.

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