Injectafer is an iron replacement product indicated for the treatment of iron deficiency anemia (IDA) in adult patients.

- who have intolerance to oral iron or have had unsatisfactory response to oral iron, or
- 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 recurs. (2)

**Dosage Forms and Strengths**

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

**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)
- 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 Injectafer administration. (5.3)

**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.

*Sections or subsections omitted from the full prescribing information are not listed.*
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 occurred mostly after repeated exposure to Injectafer in patients with no reported history of renal impairment. Possible risk factors for hypophosphatemia include a history of gastrointestinal disorders associated with malabsorption of fatsoluble 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 [see Dosage and Administration (2.3)].

5.3 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)].

5.4 Laboratory Test Alterations
In the 24 hours following administration of Injectafer, laboratory assays may oversestimate 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 [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.

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

<table>
<thead>
<tr>
<th>Term</th>
<th>Injectafer (N=1,775) %</th>
<th>Pooled Comparators a (N=1,783) %</th>
<th>Oral Iron (N=253) %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>7.2</td>
<td>1.8</td>
<td>1.2</td>
</tr>
<tr>
<td>Hypertension</td>
<td>3.8</td>
<td>1.9</td>
<td>0.4</td>
</tr>
<tr>
<td>Flushing/Hot Flush</td>
<td>3.6</td>
<td>0.2</td>
<td>0.0</td>
</tr>
<tr>
<td>Blood Phosphorus Decrease</td>
<td>2.1</td>
<td>0.1</td>
<td>0.0</td>
</tr>
<tr>
<td>Dizziness</td>
<td>2.0</td>
<td>1.2</td>
<td>0.0</td>
</tr>
<tr>
<td>Vomiting</td>
<td>1.7</td>
<td>0.5</td>
<td>0.4</td>
</tr>
<tr>
<td>Injection Site Discoloration</td>
<td>1.4</td>
<td>0.3</td>
<td>0.0</td>
</tr>
<tr>
<td>Headache</td>
<td>1.2</td>
<td>0.9</td>
<td>0.0</td>
</tr>
<tr>
<td>Alanine Aminotransferase Increase</td>
<td>1.1</td>
<td>0.2</td>
<td>0.0</td>
</tr>
<tr>
<td>Dysgeusia</td>
<td>1.1</td>
<td>2.1</td>
<td>0.0</td>
</tr>
<tr>
<td>Hypotension</td>
<td>1.0</td>
<td>1.9</td>
<td>0.0</td>
</tr>
<tr>
<td>Constipation</td>
<td>0.5</td>
<td>0.9</td>
<td>3.2</td>
</tr>
</tbody>
</table>

 survival 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 an 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 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 postnatal 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.

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. However, the data do not inform the full potential exposure of iron for the breastfed infant. Among the breastfed infants, there were no adverse events reported that 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.

Clinical Considerations
Monitor breastfed infants for gastrointestinal toxicity (constipation, diarrhea).

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.
Injection of Injectafer (ferric carboxymaltose injection) is a dark brown, sterile, aqueous, isotonie colloidal solution for intravenous injection. Each mL contains 50 mg iron as ferric carboxymaltose in water for injection. Injectafer is available in 15 mL single-dose vials. Sodium hydroxide 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.

12.2 Pharmacodynamics

Using positron emission tomography (PET) it was demonstrated that red cell uptake of $^{59}$Fe and $^{58}$Fe from Injectafer ranged from 61% to 99%. In patients with iron deficiency, red cell uptake of radio-labeled iron ranged from 91% to 99% at 24 days after Injectafer dose. In patients with renal anemia, red cell uptake of radio-labeled 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 1000 mg of iron in iron deficient patients, maximum iron concentration of 37 µg/mL to 333 µg/mL were observed at 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.

Table 2 shows the baseline and the change in hemoglobin from baseline to highest value between baseline and Day 35 or time of intervention.

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

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 mutagenesis assay in mouse lymphoma L5178Y/Tk+/- cells, in vivo mouse micronuclei 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. The dose of 30 mg/kg in animals is approximately 40% of the human dose of 750 mg based on body surface area.

14. CLINICAL STUDIES

14.1 Trial 1: Iron Deficiency Anemia in Patients Who Are Intolerant to Oral Iron or Have Had Unsatisfactory Response to Oral Iron

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 1500 mg of iron.
INJECTAFER (in-jeckt-a-fer)
(ferric carboxymaltose injection)

What is INJECTAFER?
INJECTAFER is a prescription iron replacement medicine used to treat iron deficiency anemia (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.

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  • low levels of phosphorous in your blood
• flushing  • 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.

AMERICAN REGENT, INC.
SHIRLEY, NY 11967

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.
Revised: 9/2020