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

----------RECENT MAJOR CHANGES----------

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

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

Injectafer 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 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. For adult patients weighing 50 kg or more, an alternative dose of 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.

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

----------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

----------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)
- **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 in adults (>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.*

----------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: 11/2021

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

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

Each mL of Injectafer contains 50 mg of elemental iron.

2.2 Preparation and Administration

Administer Injectafer 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, 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 1,000 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.

2.3 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 *[see Warnings and Precautions (5.2)]*.

3 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

4 CONTRAINDICATIONS

Injectafer is contraindicated in patients with a history of 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% (2/1,775) 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 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 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 *[see Dosage and Administration (2.3)]*.

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 [*see Dosage and Administration (2)*].

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 *[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 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

	Injectafer **(N=1,775)** **%**	**Pooled Comparators[a]** **(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

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

*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 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 1VIT07017 (NCT00548860) and 1VIT07018 (NCT00548691) with a dosing regimen of Injectafer 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 Injectafer 15 mg/kg to a Maximum of 1,000 mg.

	Injectafer 15 mg/kg to a maximum of 750 mg x 2 doses to a cumulative dose of 1,500 mg	**Injectafer 15 mg/kg to a maximum of 1,000 mg single dose**
	IVIT09030 and IVIT09031[b] (n=1,775) %	**IVIT07017 and IVIT07018[a](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

DOCKET ALARM

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