Leading the way in iron replacement therapy

There is no replacement for experience.
Indication | Injectafer® (ferric carboxymaltose injection) | Venofer® (iron sucrose injection, USP)
--- | --- | ---
Iron deficiency anemia (IDA) in adult patients who have non-dialysis dependent chronic kidney disease (NDD-CKD) | ✔ | ✔
IDA in patients with peritoneal-dialysis dependent (PDD) or hemodialysis dependent (HDD) CKD | ✔ | ✔
IDA in adult patients who have intolerance to oral iron or have had unsatisfactory response to oral iron | ✔ | ✔
IDA of various etiologies, which may include*: –GI disorders –OB/GYN disorders –Cancer –Heart failure –Post-gastric bypass | ✔ | ✔
Indicated for pediatric patients (age 2 years and older) with HDD-CKD for iron maintenance treatment or with NDD-CKD or PDD-CKD who are on erythropoietin therapy for iron maintenance treatment | ✔ | ✔
Dextran-free IV iron | ✔ | ✔

**SELECTED SAFETY INFORMATION FOR INJECTAFER**

**WARNINGS AND PRECAUTIONS**

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. *Injectafer and Venofer are not indicated to treat these conditions.  †For adult patients weighing less than 50 kg (110 lb), give each dose as 15 mg/kg body weight for a total cumulative dose not to exceed 1500 mg of iron per course of treatment.  ‡When administered via IV 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 <2 mg of iron per mL and administer over at least 15 minutes. When administered as a slow IV push, give at the rate of approximately 100 mg (2 mL) per minute. Please see attached Full Prescribing Information for Injectafer and Venofer.

**SELECTED SAFETY INFORMATION FOR VENOFER**

**WARNINGS AND PRECAUTIONS**

Serious hypersensitivity reactions, including anaphylactic-type reactions, some of which have been life-threatening and fatal, have been reported in patients receiving Venofer. Patients may present with shock, clinically significant hypotension, loss of consciousness, and/or collapse. If hypersensitivity reactions or signs of intolerance occur during administration, stop Venofer immediately. Monitor patients for signs and symptoms of hypersensitivity during and after Venofer administration for at least 30 minutes and until clinically stable following completion of the infusion. Only administer Venofer when personnel and therapies are immediately available for the treatment of serious hypersensitivity reactions. Most reactions associated with intravenous iron preparations occur within 30 minutes of the completion of the infusion. Most reactions associated with intravenous iron preparations occur within 30 minutes of the completion of the infusion. *Injectafer and Venofer are not indicated to treat these conditions.  †For adult patients weighing less than 50 kg (110 lb), give each dose as 15 mg/kg body weight for a total cumulative dose not to exceed 1500 mg of iron per course of treatment.  ‡When administered via IV 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 <2 mg of iron per mL and administer over at least 15 minutes. When administered as a slow IV push, give at the rate of approximately 100 mg (2 mL) per minute. Please see attached Full Prescribing Information for Injectafer and Venofer.
The following serious adverse reactions have been most commonly reported from the post-marketing dose of 1500 mg of iron. Adverse reactions reported by ≥2% of Injectafer-treated patients were nausea (7.2%); vomiting (1.7%); headache (1.3%); hypotension (0.6%); hypertension (0.6%); dizziness (0.4%); chest pain (0.3%); peripheral edema (0.3%); and syncope (0.3%).

The top selling IV iron in the US every year since 2003:

- Over 20 million patients treated with over 417 million units prescribed worldwide.
- Wide formulary acceptance for in-hospital use.
- Multiple dosage strengths and dosing options available.
- May be administered as a slow IV push over 2-5 minutes.

Stable for 7 days:

- Syringe stability: When diluted with 0.9% NaCl at concentrations ranging from 2 mg to 10 mg of elemental iron per mL, or undiluted (20 mg elemental iron per mL) and stored in a plastic syringe, has been found to be physically and chemically stable for 7 days at controlled room temperature (25°C ± 2°C) and under refrigeration (4°C ± 2°C).
- Intravenous admixture stability: When added to intravenous infusion bags (PVC or non-PVC) containing 0.9% NaCl at concentrations ranging from 1 mg to 2 mg of elemental iron per mL, has been found to be physically and chemically stable for 7 days at controlled room temperature (25°C ± 2°C).

### SELECTED SAFETY INFORMATION FOR VENOFER ADVERSE REACTIONS

The most common adverse reactions (≥2%) following the administration of Venofer are diarrhea, nausea, vomiting, headache, dizziness, hypotension, pruritus, pain in extremity, arthralgia, back pain, muscle cramp, injection site reactions, chest pain and peripheral edema. Additional adverse reactions include infusion site pain or burning, graft complications, and nasopharyngitis, sinitis, upper respiratory tract infections and pharyngitis.

In pediatric patients, more than 50% of the patients experienced at least one treatment-emergent reaction. The most common adverse reactions (≥2%) were headache, respiratory tract viral infection, peritonitis, vomiting, pyrexia, dizziness, cough, renal transplant, nausea, arteriovenous fistula thrombosis, hypotension and hypertension.

Injection site discoloration has been reported following extravasation. Ensure stable intravenous access to avoid extravasation.

Please see attached Full Prescribing Information for Injectafer and Venofer.
To report adverse events, please contact American Regent at 1-800-734-9236. You may also contact the FDA at www.fda.gov/medwatch or 1-800-FDA-1088.

Please see attached Full Prescribing Information for Injectafer and Venofer.

Injection site discoloration has been reported in 1.0% (2/1775) of the total number of patients in two randomized clinical studies. This color change was temporary, in the majority of cases it occurred within 7 days, and persisted for a maximum of 21 days. Injection site discoloration has been reported in <1% of patients in clinical studies of Injectafer and Venofer. However, in observational studies, discoloration was reported in 1.0% (2/197) of patients. Discoloration was not associated with any sequelae that required medical treatment.

Injection site discoloration has been reported in patients treated with parenteral iron. In patients treated with 100 mg of iron (as iron sucrose), discoloration was reported in 1.2% of patients. In patients treated with 10 mg of iron (as ferric carboxymaltose), discoloration was reported in 1.5% (11/733) of patients. In patients treated with 10 mg of iron (as Venofer), discoloration was reported in 0.1% (1/972) of patients. In patients treated with 100 mg of iron (as Venofer), discoloration was reported in <0.1% of patients.

Injection site discoloration has been reported in adult patients with non-dialysis dependent chronic kidney disease. In these patients, injection site discoloration was reported in 1.0% (1/101) of patients. Injection site discoloration has been reported in pediatric patients with chronic kidney disease. In these patients, injection site discoloration was reported in 1.2% (2/166) of patients.

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Trusted options for your adult IDA patients

Which option is appropriate for your patients?

Injectafer®
ferrocyanide maltolate injection

The #1 IV iron in oncology and gastroenterology clinics*
- The only dextran-free IV iron for adult patients with IDA from etiologies other than CKD
- Over 7500 patients treated in clinical trials worldwide†
- Approved in 70 countries worldwide‡

INDICATIONS FOR INJECTAFER®
Injectafer is an iron replacement product indicated for the treatment of iron deficiency anemia in adult patients:
- who have intolerance to or have had unsatisfactory response to oral iron or
- who have non-dialysis dependent chronic kidney disease

CONTRAINDICATIONS FOR INJECTAFER
Injectafer is contraindicated in patients with hypersensitivity to Injectafer or any of its inactive components.

Venofer®
iron sucrose injection, USP

Over a decade of clinical experience‡
- The market leader for the treatment of IDA in CKD (dialysis and non-dialysis dependent)
- Consistently the #1 selling IV iron in the US§
- Wide formulary acceptance for in-hospital use

INDICATION FOR VENOFER®
Venofer is indicated for the treatment of iron deficiency anemia in patients with chronic kidney disease.

CONTRAINDICATIONS FOR VENOFER
Venofer is contraindicated in patients with known hypersensitivity to Venofer.

*Based on IMS DDD MG Sales (July 2015 to December 2015).

Please see attached Full Prescribing Information and the Important Safety Information inside for Injectafer and Venofer.

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INJECTAFER® (feric carboxymaltose injection)

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® (feric carboxymaltose injection)
For intravenous use.
Initial U.S. Approval: 2013

INDICATIONS AND USAGE
Injectafer is a powder for reconstitution to be administered in reconstituted solution for intravenous use.

DOSE AND ADMINISTRATION
Reconstitute vials with 2.5 mL of preservative-free sterile water for injection. Draw 14.7 mL into a syringe and administer the reconstituted solution over 5 to 10 minutes through a 16- or 18-gauge peripheral intravenous line. Caution should be exercised to avoid extravasation, as severe local tissue damage can occur. The reconstituted solution is physically and chemically stable for 72 hours when stored at room temperature. When mixed with 25% dextrose in water, the reconstituted solution is chemically stable for 24 hours. The reconstituted solution should be administered as soon as possible after reconstitution. Do not administer to patients with a history of known hypersensitivity to Injectafer or any of its excipients.

CONTRAINDICATIONS
Injectafer is contraindicated in patients who have a known hypersensitivity to Injectafer or any of its excipients.

WARNINGS AND PRECAUTIONS
The following warnings and precautions should be considered when using Injectafer.

1. Hypersensitivity: Severe 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. At least 30 minutes and until clinically stable following completion of the infusion. Only administer Injectafer when personnel and therapy are immediately available for the treatment of serious hypersensitivity reactions. (See Adverse Reactions (6.1 and 6.2)).

2. NURSING MOTHERS: Exercise caution when administered to a nursing mother.

3. ADVERSE REACTIONS
In clinical trials, serious adverse reactions were reported in 0.1% (21/775) of subjects receiving Injectafer. Other serious or severe adverse reactions potentially associated with hypersensitivity included hypotension, flushing, urticaria, angioedema, or anaphylaxis. For hypersensitivity reactions, the adverse reactions observed were similar to those usually associated with iron administration, including rash, urticaria, angioedema, hypotension, syncope, and anaphylaxis.

4. ADVERSE REACTIONS
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-dysplastic dependent chronic kidney disease.

5. DOSAGE AND ADMINISTRATION
For patients weighing 50 kg (110 lb) or more: 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 AND STRENGTHS
The following table shows the available strengths:

<table>
<thead>
<tr>
<th>Term</th>
<th>Injectafer Pooled Comparatora</th>
<th>Oral iron</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=1775</td>
<td>N=1783</td>
<td>N=253</td>
</tr>
<tr>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>Adverse Reactions</td>
<td>Hypersensitivity</td>
<td>0.1</td>
</tr>
<tr>
<td></td>
<td>Hypotension</td>
<td>2.0</td>
</tr>
<tr>
<td></td>
<td>Urticaria</td>
<td>2.0</td>
</tr>
<tr>
<td></td>
<td>Angioedema</td>
<td>2.0</td>
</tr>
<tr>
<td></td>
<td>Hypersensitivity reaction</td>
<td>2.0</td>
</tr>
<tr>
<td></td>
<td>Death</td>
<td>0.1</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>2.0</td>
</tr>
</tbody>
</table>

6. DRUG INTERACTIONS
In clinical studies, serious anaphylactic/anaphylactoid reactions were reported in 1.5% (26/1775) of these subjects. Hypersensitivity reactions were reported in 1.5% (26/1775) of these subjects.

7. LABORATORY TEST ALTERATIONS
In clinical studies, hypertension was reported in 3.8% (67/1775) of subjects in clinical trials 1 and 2. Transient elevations in systolic blood pressure, sometimes occurring with facial flushing, dizziness, or nausia 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)).

8. USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
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-dysplastic dependent chronic kidney disease.

8.2 Geriatric Use
In clinical studies, serious anaphylactic/anaphylactoid reactions were reported in 1.5% (26/1775) of these subjects. Hypersensitivity reactions were reported in 1.5% (26/1775) of these subjects.

8.3 Nursing Mothers
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-dysplastic dependent chronic kidney disease.

8.4 Pediatric Use
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-dysplastic dependent chronic kidney disease.

8.5 Geriatric Use
In clinical studies, serious anaphylactic/anaphylactoid reactions were reported in 1.5% (26/1775) of these subjects. Hypersensitivity reactions were reported in 1.5% (26/1775) of these subjects.

9. DRUG ABUSE AND DEPENDENCE
Injectafer is not known to be habit forming.

10. OVERDOSAGE
10.1 Description
A post-marketing experience

11. DESCRIPTION
Ferumoxytol, an iron replacement product, is an iron carbohydrate complex with the chemical name of polymeric iron (III) hydroxide (4·(C6H12O8))·D-glucuronic acid (D-α-D-glucuronic acid-β-D-galactopyranosyl-α-D-glucopyranosyl-β-D-glucopyranosyl-hexaose). It has a relative molecular weight of approximately 150,000 Da corresponding to the following empirical formula:

\[ (C6H12O8)_n \cdot D-glucuronic acid \] where \( n = 10 \), \( m = 8 \), \( b = 11 \), and \( k = 4 \) (i represents the mean branching degree of the ligand).

The chemical structure is presented below:

(\[ C16H24O10 \]) \[ 1.0 \times 10^6 \]
INJECTAFER®
(ferric carboxymaltose injection)

Injectaferr (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. Injectaferr is available in 15 mL, single-use 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 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 position emission tomography (PET) it was demonstrated that red cell uptake of 114mCr and 111In from Injectaferr ranged from 60% to 90%. In patients with iron deficiency, red cell uptake of radio-labeled iron ranged from 90% to 95% at 24 days after Injectaferr dose. In patients with renal anemia red cell uptake of radio-labeled iron ranged from 61% to 84% after 24 days Injectaferr dose.

12.3 Pharmacokinetics
After administration of a single dose of Injectaferr of 100 to 1000 mg of iron in iron deficient patients, maximum iron levels of 37 μg/mL to 333 μg/mL were obtained respectively after 15 minutes to 1.21 hours post-dose. Peak volume distribution was estimated to be 3 L.

The iron injected was rapidly cleared from the plasma, the terminal half-life ranged 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 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/T-1 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 once 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 body weight based on surface area.

14 CLINICAL STUDIES

The safety and efficacy of Injectaferr for treatment of iron deficiency anemia were evaluated in two randomized, open-label, controlled clinical trials (Trial 1 and Trial 2). In these two trials, Injectaferr 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.

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

Trial 1 was a randomized, open-label, controlled clinical study in patients with iron deficiency anemia 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) <11 g/dL, ferritin ≤100 ng/mL, or ferritin ≤300 ng/mL when transferrin saturation (TSAT) ≤30%. Cohort 1 subjects were randomized to Injectaferr or oral iron for 14 more days. Cohort 2 subjects were randomized to Injectaferr or another IV iron per standard of care (90% of subjects received iron sucrose). The mean age of study patients was 45 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 iron deficiency anemia were heavy uterine bleeding (47%) and gastrointestinal disorders (17%).

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

![Table 2](image-url)

14.2 Trial 2: Iron Deficiency Anemia in Patients with Non-Dialysis Dependent Chronic Kidney Disease

Trial 2 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 Injectaferr or Venletat. The mean age of study patients was 67 years (range, 19 to 96); 64% were female; 54% were Caucasian, 26% were African American, 18% Hispanics, and 2% were other races.

Table 3 shows the baseline and the change in hemoglobin from baseline to highest value between baseline and Day 35 of time of intervention.

![Table 3](image-url)

INJECTAFER®
(ferric carboxymaltose injection)

Please read this information carefully before taking this medication. This summary does not tell you everything about INJECTAFER. Speak with your doctor or healthcare professional if there is something you do not understand or if you would like to learn more about INJECTAFER. Your doctor or healthcare professional is your best source of information about this medicine.

What is INJECTAFER®?

Iron is a mineral that the body needs to produce red blood cells. When the body does not get enough iron, it cannot produce the number of normal red blood cells needed to keep you in good health. This condition is called iron deficiency (iron shortage) or iron deficiency anemia.

INJECTAFER® is used to treat iron deficiency anemia. Iron deficiency anemia may be caused by several medical conditions including heavy menstrual bleeding, pregnancy, inflammatory bowel disease, other malabsorption disorders, bariatric surgery, or chronic kidney disease.

General information about using INJECTAFER safely and effectively

Injectable iron is administered only by or under the supervision of your health care professional. Serious or life threatening allergic reactions have been reported with intravenous iron products. Tell your health care professional if you have ever had any unusual or allergic reaction to any IV iron.

Patients should report to their healthcare professional any signs and symptoms of an allergic reaction to INJECTAFER, in particular rashes, shortness of breath and wheezing.

Iron should not be administered from the bottle, and its build up may lead to a condition called iron overload which may be harmful. Certain medical conditions such as liver disease may also make you more likely to develop iron overload. Ask your doctor or healthcare professional.

Who should not take INJECTAFER®?

You should not be given INJECTAFER® if you have anemia that is not caused by iron deficiency, or if you have iron overload.

If you are pregnant or plan to become pregnant please notify your doctor or healthcare professional. They will decide whether it is safe for you to receive INJECTAFER®.

How should I take INJECTAFER®?

INJECTAFER® is administered intravenously (into your vein) by your doctor or healthcare professional in two doses.

Who should avoid while taking INJECTAFER®?

You should not take iron supplements by mouth if you are receiving iron injections. Tell your doctor about all the medications you take, including prescription and non-prescription medicines, vitamins and herbal supplements.

What are the possible side effects of INJECTAFER®?

The side effects of INJECTAFER® are infrequent, usually mild and generally do not cause patients to stop treatment. The most common side effects are nausea, injection site reactions (including pain or bruising at the injection site), asymptomatic reductions in blood phosphorus, flushing, headache, hypertension, dizziness, and increased alanine aminotransferase. Potentially long lasting brown staining of skin and injection site may occur.

These are not all the possible side effects of INJECTAFER®. For more information ask your doctor or healthcare professional. Talk to your doctor if you think you have side effects from taking INJECTAFER®.
**Dosage and Administration**

**Venofer**

**DOSAGE AND ADMINISTRATION**

- **Hemodialysis Dependent-Chronic Kidney Disease (HDD-CKD)**
  - In adult patients with HDD-CKD, administer Venofer 300 mg or 400 mg intravenous infusion over 15 minutes.
  - The dosing for iron replacement treatment in pediatric patients with HDD-CKD has not been established.

**Non-Hemodialysis Dependent-Chronic Kidney Disease (NDD-CKD)**

1. Adult Patients with Non-Hemodialysis Dependent-Chronic Kidney Disease (NDD-CKD)
   - Administer Venofer 200 mg unverified as a slow intravenous injection over 2 to 5 minutes or as an intravenous injection of 200 mg in a maximum of 100 mL of 0.9% NaCl over a period of at least 15 minutes, per consecutive hemodialysis session. Venofer should be administered during or following the dialysis session. The usual total dose of Venofer is 1000 mg. Venofer treatment may be repeated if iron deficiency recurs.

2. Pediatric Patients with Non-Hemodialysis Dependent-Chronic Kidney Disease (PDD-CKD)
   - Venofer 200 mg unverified as a slow intravenous injection over 2 to 5 minutes or as an intravenous injection of 200 mg in a maximum of 100 mL of 0.9% NaCl over a period of 3.5 to 4 hours on Day 1 and Day 14. Venofer treatment may be repeated if iron deficiency recurs.

**Pediatric Patients (2 years of age and older) with NDD-CKD or PDD-CKD who are on erythropoietin therapy for iron maintenance treatment**

- Administer Venofer at a dose of 0.5 mg/kg, not to exceed 100 mg per dose, every four weeks for 12 weeks given unverified by slow intravenous injection over 5 minutes or diluted in 25 mL of 0.9% NaCl and administered over 5 to 60 minutes. Venofer treatment may be repeated if necessary.

**2.5 mL single-use vial / 50 mg elemental iron (20 mg/mL)**

**5 mL single-use vial / 100 mg elemental iron (20 mg/mL)**

**10 mL single-use vial / 200 mg elemental iron (20 mg/mL)**

**4.1 Hypersensitivity Reactions**

- Venofer must only be administered intravenously either by slow injection or by infusion. The dose of Venofer is expressed in mg of elemental iron.

**1.12 Shake well before using**

**5.6 Iron Overload**

- Regularly monitor hematologic responses during Venofer therapy. Do not administer Venofer to patients with iron overload.

**1.12 Shake well before using**

**5.6 Iron Overload**

- In patients with iron overload, the risk of iron overload is increased when treatment is initiated with iron stores above normal limits.

**1.12 Shake well before using**

**6. ADVERSE REACTIONS**

- The frequency of adverse reactions associated with the use of Venofer has been documented in six clinical trials involving 231 patients treated with Venofer in clinical trials for which the rate for Venofer exceeds the rate for comparator are listed by indication in Table 1.

**5.6.1 Adverse Reactions in Clinical Trials**

- Treatment-emergent adverse reactions reported by treated patients in the six clinical trials for which the rate for Venofer exceeds the rate for comparator are listed by indication in Table 1.

**5.6.1 Adverse Reactions in Clinical Trials**

- The rate of treatment-emergent adverse reactions reported by treated patients in the six clinical trials for which the rate for Venofer exceeds the rate for comparator are listed by indication in Table 1.

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- The rate of treatment-emergent adverse reactions reported by treated patients in the six clinical trials for which the rate for Venofer exceeds the rate for comparator are listed by indication in Table 1.

**5.6.1 Adverse Reactions in Clinical Trials**

- The rate of treatment-emergent adverse reactions reported by treated patients in the six clinical trials for which the rate for Venofer exceeds the rate for comparator are listed by indication in Table 1.
Adverse Reactions in Pediatric Patients with CKD (ages 2 years and older)

Adverse reactions were similar in severity and type in patients treated with Venofer in pediatric patients with CKD on stable erythropoietin therapy (see Clinical Studies (14)). At least one treatment-emergent adverse reaction was reported in 57% (274/480) of the Venofer patients and 57% (285/500) of the patients receiving placebo. The most common treatment-emergent adverse reactions were injection site reactions (0.5% of patients receiving Venofer and 0.4% of patients receiving placebo) and worsening cardiac failure (0.4% of patients receiving Venofer and 0.2% of patients receiving placebo).

1.3.1.1 Hematological

Venofer 100 mg was used at 10 consecutive dialysis sessions either as slow injection or a slow infusion. The historical control population consisted of 51 patients treated with placebo intravenous iron sucrose at 50 mg elemental iron per session over a 12-week period. Venofer 100 mg was administered intravenously to 28 patients (14 males, 14 females) who had received iron sucrose at 50 mg on three sessions at a single study site. Venofer 50 mg and Venofer 100 mg were given in a random order at 12-week intervals. During the study, the iron sucrose was used in the historical control population at 50 mg elemental iron per infusion. The mean age of the patients in the historical control population was 50 years, with a range of 21 to 70 years. The mean hemoglobin level was 8.9 g/dL at the beginning of the study. After 12 weeks, the mean hemoglobin level was 10.4 g/dL in the historical control population. After 24 weeks, the mean hemoglobin level was 10.3 g/dL in the historical control population.

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