Venofer is an iron replacement product indicated for the treatment of iron deficiency anemia (IDA) in patients with chronic kidney disease (CKD). (1)

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**DOSE AND ADMINISTRATION**

- **Adult patients**
  - Hemoglobin-Dependent Chronic Kidney Disease (HDD-CKD) (2.2)
    - 100 mg slow intravenous injection or infusion
  - Non-Hemoglobin-Dependent Chronic Kidney Disease (PDD-CKD) (2.3)
    - 200 mg slow intravenous injection or infusion
  - Peritoneal Dialysis Dependent-Chronic Kidney Disease (PDD-CKD) (2.4)
    - 300 mg 400 mg slow intravenous injection or infusion

- **Pediatric patients**
  - HDD-CKD (2.5), PDD-CKD or RDD-CKD (2.6)
    - 0.5 mg/kg slow intravenous injection or infusion

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**RECEIVING VENOFER**

- Venofer treatmen may be repeated if iron deficiency reoccurs.

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**WARNINGS AND PRECAUTIONS**

- **Hypotension:** May cause hypotension. Monitor for signs and symptoms of hypotension during and after Venofer administration for at least 30 minutes and until clinically stable following completion of each administration. Only administer Venofer when personnel and therapies are immediately available for the treatment of serious hypotensive reactions. (5.1)
- **Hypersensitivity:** React to Venofer. Observe for signs and symptoms of hypersensitivity during and after Venofer administration.
- **Iron Overload:** Do not administer to patients with iron overload. (5.3)

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**ADVERSE REACTIONS**

- **Adverse Reactions Observed During Clinical Trials:**
  - Headache, respiratory tract viral infection, pyrexia, vomiting, pyrexia, dizziness, cough, nausea, arthralgia, skin rash, hypotension, and peripheral edema. (8.1)
- **Pediatric patients:** The most common adverse reactions (≥2%): headache, respiratory tract viral infection, pyrexia, vomiting, pyrexia, dizziness, cough, nausea, arthralgia, skin rash, hypotension, and peripheral edema. (6.1)

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To report SUSPECTED ADVERSE REACTIONS, contact American Regent, Inc. at 1-800-734-9236 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

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See 17 for PATIENT COUNSELING INFORMATION.
Adverse Reactions in Pediatric Patients with CKD (ages 2 years and older)

In a randomized, open-label, dose-ranging trial for iron maintenance treatment with Venofer in pediatric patients with CKD on stable erythropoietin therapy (HDD-CKD; 18 patients, including 10 females and 8 males; age range 1 to 18 years), 70.4% of the patients received Venofer 1 mg/kg and 29.6% received Venofer 0.5 mg/kg for 2 weeks and then every other week for 8 weeks. The mean number of treatment weeks was 16.2 weeks (range: 4 to 22 weeks). The mean change (± SD) from baseline to the highest hemoglobin value was 1.2 ± 0.4 g/dL in the Venofer group and 0 g (± 0) in the control group. The mean change in ferritin (± SD) was 109 ± 49 ng/mL in the Venofer group and 19 ± 16 ng/mL in the control group. The mean change in TSAT (± SD) was 34% ± 11% in the Venofer group and 9% ± 14% in the control group. In the Venofer group, 19 patients had a change in ferritin of ≥25% at any time during the study compared to the baseline ferritin value of these patients.

13. HEMOLYTIC THERAPY

13.1 Controversies, Mitigation, Impaired of Fertility

Cancer has been associated with decreased fertility. Some studies have suggested that decreased fertility may be related to the tumor type and stage of disease.

14. CLINICAL STUDIES

14.1 Clinical Studies Overview

Five clinical trials involving 877 adult patients and one clinical trial involving 121 pediatric patients were conducted to assess the safety and efficacy of Venofer.

14.2 Study A: Hemodialysis Dependent-Chronic Kidney Disease (HDD-CKD)

Study A (NCT02065187) was a randomized, open-label, dose-ranging trial involving 131 patients (55 females and 76 males; age range 16 to 86 years). Patients with HDD-CKD with or without erythropoietin therapy were randomized to receive oral iron (325 mg ferrous sulfate per day) or Venofer once every other week. Patients received a loading dose of 10 mg iron/kg at study entry and then received a maintenance dose of 5 mg iron/kg every other week. Patients enrolled in this study were 41 years of age, with ages ranging from 16 to 70 years. Of 131 patients evaluated for efficacy, 39 patients had a change in ferritin of ≥25% at any time during the study compared to the baseline ferritin value of these patients. In the oral iron group, mean change (± SD) from baseline to the highest ferritin value was 427 ± 220 ng/mL and mean change in hemoglobin was 0.4 ± 0.3 g/dL. In the Venofer group, mean change in ferritin was 515 ± 490 ng/mL and mean change in hemoglobin was 1.2 ± 0.4 g/dL. In the Venofer group, 19 patients had a change in ferritin of ≥25% at any time during the study compared to the baseline ferritin value of these patients.

14.3 Study B: Hemodialysis Dependent-Chronic Kidney Disease (HDD-CKD)

Study B (NCT02173308) was a randomized, open-label, dose-ranging trial involving 188 patients (68 females and 120 males; age range 16 to 86 years). Patients with HDD-CKD, hemoglobin of 11.0 g/dL, transferrin saturation ≤25%, ferritin ≤300 ng/mL, enrolled in this study were 41 years of age, with ages ranging from 16 to 70 years. Of 188 patients evaluated for efficacy, 71 patients had a change in ferritin of ≥25% at any time during the study compared to the baseline ferritin value of these patients. In the oral iron group, mean change (± SD) from baseline to the highest ferritin value was 427 ± 220 ng/mL and mean change in hemoglobin was 0.4 ± 0.3 g/dL. In the Venofer group, mean change in ferritin was 515 ± 490 ng/mL and mean change in hemoglobin was 1.2 ± 0.4 g/dL. In the Venofer group, 19 patients had a change in ferritin of ≥25% at any time during the study compared to the baseline ferritin value of these patients.

14.4 Study C: Hemodialysis Dependent-Chronic Kidney Disease (HDD-CKD)

Study C (NCT03555048) was a randomized, open-label, dose-ranging trial involving 130 patients (44 females and 86 males; age range 16 to 86 years). Patients with HDD-CKD, hemoglobin of 11.0 g/dL, transferrin saturation ≤25%, ferritin ≤300 ng/mL, enrolled in this study were 41 years of age, with ages ranging from 16 to 70 years. Of 130 patients evaluated for efficacy, 56 patients had a change in ferritin of ≥25% at any time during the study compared to the baseline ferritin value of these patients. In the oral iron group, mean change (± SD) from baseline to the highest ferritin value was 427 ± 220 ng/mL and mean change in hemoglobin was 0.4 ± 0.3 g/dL. In the Venofer group, mean change in ferritin was 515 ± 490 ng/mL and mean change in hemoglobin was 1.2 ± 0.4 g/dL. In the Venofer group, 19 patients had a change in ferritin of ≥25% at any time during the study compared to the baseline ferritin value of these patients.

14.5 Study D: Peritoneal Dialysis Dependent-Chronic Kidney Disease (PD D-CKD)

Study D (NCT01399019) was a randomized, open-label, dose-ranging trial involving 130 patients (66 females and 64 males; age range 18 to 86 years). Patients with PD D-CKD, hemoglobin of 10.0 g/dL were enrolled in this study at age 41 years, with ages ranging from 18 to 86 years. Of 130 patients evaluated for efficacy, 55 patients had a change in ferritin of ≥25% at any time during the study compared to the baseline ferritin value of these patients. In the oral iron group, mean change (± SD) from baseline to the highest ferritin value was 427 ± 220 ng/mL and mean change in hemoglobin was 0.4 ± 0.3 g/dL. In the Venofer group, mean change in ferritin was 515 ± 490 ng/mL and mean change in hemoglobin was 1.2 ± 0.4 g/dL. In the Venofer group, 19 patients had a change in ferritin of ≥25% at any time during the study compared to the baseline ferritin value of these patients.

14.6 Study E: Peritoneal Dialysis Dependent-Chronic Kidney Disease (PD D-CKD)

Study E (NCT01399027) was a randomized, open-label, multi-center trial comparing patients with PD D-CKD receiving iron sucrose and iron chelator. Patients with PD D-CKD were randomized to receive iron sucrose (500 mg elemental iron every other week) or iron chelator (500 mg elemental iron every other week) for 16 weeks. The mean age of the patients in the study was 55 years, with ages ranging from 18 to 86 years. Of 131 patients evaluated for efficacy, 68 patients had a change in ferritin of ≥25% at any time during the study compared to the baseline ferritin value of these patients. In the iron sucrose group, mean change (± SD) from baseline to the highest ferritin value was 515 ± 490 ng/mL and mean change in hemoglobin was 1.2 ± 0.4 g/dL. In the iron chelator group, mean change in ferritin was 427 ± 220 ng/mL and mean change in hemoglobin was 0.4 ± 0.3 g/dL. In the iron sucrose group, 19 patients had a change in ferritin of ≥25% at any time during the study compared to the baseline ferritin value of these patients.