RXADVANCE
2 Park Central Drive
Southborough, MA 01772

NEW DRUG APPROVAL

Brand Name	Monoferric®
Generic Name	ferric derisomaltose
Drug Manufacturer	Pharmacosmos Therapeutics Inc

New Drug Approval

FDA Approval Date: January 16, 2020

Monoferric® 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; or
- who have non-hemodialysis dependent chronic kidney disease.

Review Designation: None

Review Type: Type 5 - New Formulation or New Manufacturer, NDA (208171)

Dispensing Restrictions: None

Place in Therapy

DISEASE DESCRIPTION & EPIDEMIOLOGY

Anemia is defined as hemoglobin below two standard deviations of the mean for the age and gender of the patient. Iron is an essential component of the hemoglobin molecule. The most common cause of anemia worldwide is iron deficiency, which results in microcytic and hypochromic red cells on the peripheral smear. Several causes of iron deficiency vary based on age, gender, and socioeconomic status. The patient often will have nonspecific complaints such as fatigue and dyspnea on exertion. Treatment is a reversal of the underlying condition as well as iron supplementation. Iron supplementation is most often oral, but certain cases may require intravenous iron.

Approximately 25% of people worldwide have anemia. Iron deficiency, the most common cause, is responsible for 50% of all anemias. The rate of iron deficiency is higher in developing countries compared to the United States, where the prevalence of iron-deficiency anemia in men under 50 is 1%. In women of childbearing age in the United States, the rate is 10% due to losses from menstruation, while 9% of children ages 12 to 36 months are iron-deficient, and one-third of these children develop anemia. While the rate of iron-deficiency anemia is low in the United States, low-income families are particularly at risk.

Efficacy

The safety and efficacy of Monoferric® for treatment of IDA were evaluated in two randomized, open-label clinical trials with active control (FERWON studies) performed in a total of 3,050 patients with IDA of different etiologies. Trial 1 (FERWON-IDA) included patients with IDA who had intolerance to oral iron or who had had unsatisfactory response to oral iron or for whom there was a clinical need for rapid repletion of iron stores. Trial 2 (FERWON-NEPHRO) included patients with IDA who had non-dialysis dependent chronic kidney disease. In these two 8-week trials, patients were randomized 2:1 to treatment with Monoferric® or iron sucrose. Monoferric® was intravenously administered as a single dose of 1,000 mg.

In Trial 1, 1512 adult patients with IDA caused by different etiologies were randomized in a 2:1 ratio to treatment with Monoferric® or iron sucrose. The efficacy of Monoferric® was established based upon the change in Hb from baseline to week 8. Non-inferiority was demonstrated for change in Hb from baseline to Week 8. Patients in both

arms of this study experienced a mean change in hemoglobin of 2.49 g/dL from baseline to week 8. These increases were statistically significant.

Trial 2 enrolled 1,538 patients with NDD-CKD. The efficacy of Monoferric® was established based upon the demonstration of non-inferiority for change in hemoglobin from baseline to week 8. Patients receiving Monoferric® experienced a mean increase in hemoglobin from baseline to week 8 of 1.22 g/dL, and patients treated with iron sucrose experienced a mean increase in hemoglobin from baseline to week 8 of 1.14 g/dL. Based upon these results, non-inferiority was confirmed.

In Trial 1 and Trial 2 combined, adverse reactions were reported in 8.6% of patients treated with Monoferric®. The most common adverse reactions reported were nausea (1.2%) and rash (1.0%). Adjudicated serious or severe hypersensitivity reactions were reported in 6/2,008 (0.3%) patients in the Monoferric® group.

In the full, global development program, Monoferric® has been evaluated in twenty-five clinical trials enrolling more than 5,800 patients.

Safety

ADVERSE EVENTS

Most commonly reported adverse reactions (incidence ≥1%) are rash and nausea.

WARNINGS & PRECAUTIONS

Hypersensitivity Reactions: Monitor patients for signs and symptoms of hypersensitivity during and after Monoferric® administration for at least 30 minutes and until clinically stable following completion of the infusion.

Iron Overload: Do not administer Monoferric® to patients with iron overload.

CONTRAINDICATIONS

Serious hypersensitivity to Monoferric® or any of its components.

Clinical Pharmacology

MECHANISMS OF ACTION

Ferric derisomaltose is a complex of iron (III) hydroxide and derisomaltose, an iron carbohydrate oligosaccharide that releases iron. Iron binds to transferrin for transport to erythroid precursor cells to be incorporated into hemoglobin.

Dose & Administration

ADULTS

Iron-deficiency anemia: IV:

- Weight less than 50 kg: 20 mg/kg as a single dose; may repeat if iron-deficiency anemia reoccurs.
- Weight 50 kg or more: 1,000 mg as a single dose; may repeat if iron-deficiency anemia reoccurs.

PEDIATRICS

Safety and efficacy have not been established.

GERIATRICS

Refer to adult dosing.

RENAL IMPAIRMENT

Specific guidelines for dosage adjustments in renal impairment are not available; it appears that no dosage adjustments are needed.

HEPATIC IMPAIRMENT

Specific guidelines for dosage adjustments in hepatic impairment are not available; it appears that no dosage adjustments are needed.

Product Availability

DOSAGE FORM(S) & STRENGTH(S)

- Injection: 1,000 mg iron /10 mL (100 mg/mL) single-dose vial
- Injection: 500 mg iron/5 mL (100 mg/mL) single-dose vial
- Injection: 100 mg iron/mL single-dose vial