

IV Iron Products

For any patient with any disorder where oral iron is unable or unlikely to work, IV iron is administered. There are six IV iron preparations currently on the US pharmacopoeia. Two new intravenous irons have been approved in the US, ferumoxytol and ferric carboxymaltose, permitting larger doses of iron to be administered as a single dose for more rapid iron replenishment. A discussion of each of these preparations follows.

There are six intravenous preparations of iron available.

- Iron Dextran – InFed by Watson (low molecular weight) (50 mg elemental iron per ml)
- Iron Dextran -Dexferrum (high molecular weight) by American Regent (50 mg elemental iron per ml)
- Iron Sucrose - Venofer by American Regent (20 mg elemental iron per ml)
- Sodium Ferric Gluconate – Ferrlecit by Sanofi-Aventis (12.5 mg elemental iron per ml)
- Ferumoxytol – Feraheme by AMAG (30mg elemental iron/ml)
- Ferric Carboxymaltose - Injectafer by American Regent (50mg elemental iron /mL)

Complete dosing information can be found in the IV Iron Product Chart

Iron Dextran

In 1991, low-molecular-weight iron dextran marketed as INFeD was approved for clinical use in the United States. In 1996, high-molecular-weight iron dextran marketed as Dexferrum was approved and provided an alternative to INFeD. These two products replaced Imferon (Fisons, Rochester, NY), which was no longer manufactured, for the treatment of iron deficiency anemia in patients when oral iron administration is unsatisfactory or impossible.¹

The dextran carbohydrate shell found in some iron dextran products is associated with severe immunologic responses, sometimes resulting in anaphylaxis and death. Iron dextran carries a black box warning because of this risk of severe, sometimes fatal anaphylactic reactions (loss of consciousness, collapse, difficulty breathing,

severe hypotension). A test dose is required prior to use.^{2,3}

Current information suggests that low-molecular-weight iron dextran is associated with a markedly lower risk of serious adverse events than high-molecular-weight iron dextran, with a serious adverse event rate of less than 1:200,000.¹ Immediate reactions have occurred in 3% to 7% of patients, and life-threatening reactions have occurred in 0.6% to 1.3% of patients using high molecular weight IV iron dextran.⁴ Based on the preponderance of published literature, if high molecular weight dextran is used, it should only be used with caution. Please note: the J-code for high molecular weight is the same as for low molecular weight iron dextran, and many pharmacists are unaware of the differences.

The total amount of iron dextran required for the treatment of iron deficiency anemia or iron replacement for blood loss is determined from the patient's body weight, current Hb level, and desired target Hb. INFeD is given undiluted at a slow gradual rate not to exceed 50 mg (1 mL) per minute.^{2,3} Although the intramuscular route of administration is approved it is painful, less effective, and therefore should be avoided. Alternatively, the total iron replacement dose of INFeD can be diluted in normal saline and administered as a single IV infusion.

The easiest, least expensive, most efficacious and probably least toxic means of correcting iron deficiency with LMW iron dextran is with a total dose infusion (TDI). We have now given approximately 400 patients 1000 mg of LMW ID in one hour. The drug is diluted in 250 ml of normal saline. The test dose can be administered as a separate IV push or as a slow infusion of the diluted material. If after 5-10 minutes no adverse reaction is seen, none will occur. The remaining dose can be administered at 250 ml per hour such that the infusion can be completed in 60 minutes. For patients with a history of multiple drug allergies, a prior sensitivity to iron dextran or asthma, 125 mg methylprednisolone should be administered prior to the test dose. Otherwise, premedication should be avoided.⁵

IRON CORNER

Although anaphylaxis has been reported with LMW ID, we have administered >70,000 doses in our practice (one dose=100 mg) without a single SAE.

However, two adverse events uncommonly occur, but may be seen. The first of these was described by Fishbane which is the acute onset of chest and back pain or tightness WITHOUT hypotension, tachypnea, tachycardia, wheezing, stridor, or periorbital edema. This harmless reaction, which never leaves residua, abates in minutes and does not recur with rechallenge. Should this reaction occur, NO TREATMENT should be administered, the patient should be reassured, observed for a few minutes, and treatment proceeded with cautiously after abatement of all symptoms.

The second adverse event which occurs in approximately 10% of patients consists of arthralgias and myalgias, usually occurring about 24 hours after the infusion. These reactions also never leave residua, abate without therapy, but more quickly when non-steroidal anti-inflammatories are administered.⁵

Iron Sucrose and Ferric Gluconate

Iron sucrose and iron ferric gluconate do not contain the dextran moiety, and the incidence of anaphylactic reactions with these products is thought to be lower. Two well done retrospective studies^{6,7} showed that serious acute events with the iron salts were far less likely to occur than with iron dextran and were safe in those previously sensitive to iron dextran. As a result of these two papers, iron sucrose and ferric gluconate rapidly replaced iron dextran in dialysis patients.

Unlike iron dextran, where the total dose can be given in a single setting, these agents can only be given in smaller doses not to exceed 200 mg of ferric gluconate and 400 mg for iron sucrose. This requires multiple visits and multiple infusions. However, for dialysis patients coming three times a week for their treatments, the need for frequent IV iron administration is not clinically or logistically relevant.⁵

Iron Sucrose⁸

Iron sucrose has been used in Europe since 1949, and was approved by the FDA in November 2000. It is

indicated for the treatment of anemia in dialysis-dependent and non-dialysis-dependent CKD patients. It is approved in both adult and pediatric patients. Both iron sucrose and ferric gluconate have been used successfully in patients who are intolerant to iron dextran. Iron sucrose has also been used successfully in patients intolerant to both iron dextran and ferric gluconate.

Ferric Gluconate⁹

Ferric gluconate was first used in Europe in 1977, was approved by the FDA for use in the United States in February 1999. It is currently indicated for the treatment of iron deficiency anemia in adult and pediatric patients undergoing chronic hemodialysis who are receiving supplemental ESA therapy. Both iron sucrose and ferric gluconate have been used successfully in patients who are intolerant to iron dextran. There are no data available on the use of ferric gluconate in patients intolerant to iron sucrose, or both iron dextran and iron sucrose.⁹

Ferumoxytol¹⁰

In June of 2009, ferumoxytol, was approved for administration to iron deficient patients with chronic renal failure. This drug is supplied in a 510 mg vial, increasing convenience by decreasing pharmacists' time for preparation. There is no data at the present time with the administration of higher doses. Therefore, complete replacement for iron deficient patients requires at least two visits. Ferumoxytol may be given as a 510 mg IV push over approximately 20-30 seconds.

However, it appears that an administration time of 60-90 seconds may be more prudent. The drug commonly causes an asymptomatic 10-12 mm drop in systolic pressure that abates without treatment or symptoms. Other adverse events are uncommon. Anaphylaxis has been reported with this drug as well as with all of the other iron compounds. In clinical studies, serious hypersensitivity reactions were reported in 0.2% (3/1726) of subjects receiving ferumoxytol. Other adverse reactions potentially associated with hypersensitivity (e.g., pruritus, rash, urticaria, or wheezing) were reported in 3.7% (63/1726) of these subjects.

The logo for 'Iron Corner' is a dark red square with the words 'IRON' and 'CORNER' stacked vertically in white, bold, sans-serif capital letters. The background of the square features a faint, light-colored molecular or network structure.

IRON CORNER

Ferric Carboxymaltose¹¹

In 2013, ferric carboxymaltose, the newest of the IV irons became available in the US. It has been used in Europe and other countries since 2009. Ferric carboxymaltose is indicated for the treatment of iron-deficiency anemia (IDA) in adults who either cannot tolerate or have not responded well to oral iron. Ferric carboxymaltose can be administered as a single dose of up to 750 mg and undiluted as an intravenous push injection at a rate of 100 mg/minute or as an intravenous infusion in up to 250 mL 0.9% sodium chloride injection over the course of at least 15 minutes. Therefore, complete replacement for iron deficient can be achieved in only one to two visits.

In clinical trials, serious anaphylactic/ anaphylactoid reactions were reported in 0.1% (2/1775) 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% (26/1775) of these subjects.

November 2013

References

1. Shander A, Spence RK, Auerbach M. Can intravenous iron therapy meet the unmet needs created by the new restrictions on erythropoietic stimulating agents? *Transfusion*. 2010 Mar;50(3):719-32.
2. DexFerrum [package insert]. Shirley, NY: American Regent; 2008.
3. InFeD [package insert]. Morristown, NJ: Watson Pharma; 2009
4. Aronoff G et al. Iron sucrose in hemodialysis patients: Safe and effective iron replacement and maintenance therapy. *Kidney Int* 2004; 66:1193-1198.
5. Auerbach M, Ballard H, Glaspy J. Clinical update: intravenous iron for anaemia. *Lancet* 2007; 369: 1502-1504.
6. Coyne DW, Adkinson NF, Nissenson AR, et al Sodium ferric gluconate complex in hemodialysis patients. II. Adverse reactions in iron dextran-sensitive and dextran-tolerant patients. *Kidney Int*. 2003 Jan;63(1):217-24.
7. Michael B, Coyne DW, Fishbane S, et al. Sodium ferric gluconate complex in hemodialysis patients: adverse reactions compared to placebo and iron dextran. *Kidney Int*. 2002 May;61(5):1830-9.
8. Venofer [package insert]. Shirley, NY, American Regent; 2012.
9. Ferrlecit [package insert]. Bridgewater, NJ: Sanofi Aventis US; 2011.
10. Injectafer [package insert]. Shirley, NY: American Regent; 2013.
11. Feraheme [package insert], Lexington, MA: AMAG Pharmaceuticals; 2012.

Disclaimer

This content is covered by an important disclaimer that can be found at www.iron.sabm.org. Please read this disclaimer carefully before reviewing this content.