



Subject: Intravenous Iron Therapy

Revision Date: 7/24

DESCRIPTION

Iron deficiency anemia (IDA) is most often caused by blood loss. However, IDA may also be the result of reduced iron absorption or redistribution after erythropoietin/erythropoiesis-stimulating agents. Treatment of the underlying cause in combination with oral iron supplementation is appropriate for most patients. Rarely, parenteral iron may be required. While parenteral iron provides a more rapid therapeutic response than oral iron, it can cause adverse effects including allergic reactions. Current parenteral iron preparations include:

- INFeD (iron dextran)
- Injectafer (ferric carboxymaltose)
- Feraheme (ferumoxytol)
- Ferrlecit (sodium ferric gluconate complex)
- Monoferric (ferric derisomaltose)
- Venofer (iron sucrose)

DEFINITIONS

Feraheme (ferumoxytol): Available as 510 mg iron per 17 mL (30 mg per mL) in single-dose vials. The recommended dose is an initial 510 mg dose followed by a second 510 mg dose 3 to 8 days later.

Ferrlecit (sodium ferric gluconate complex): Available as 62.5 mg/5 mL (12.5 mg/mL) in single-dose vials. The recommended dose for adults is 125 mg infused during each dialysis session. The recommended dose for pediatrics is 1.5 mg/kg infused during each dialysis session. Ferrlecit treatment may be repeated if iron deficiency reoccurs.

INFeD (iron dextran): Available as 100 mg/2 mL (50 mg/mL) in single-dose vials. The recommended

dose varies depending on the indication.

The dosing for anemia is based on the patient's weight and hemoglobin level. The following formula can be utilized to calculate the total dose for patients over 15 kg:

$$\text{Dose (mL)} = 0.0442 (\text{Desired Hb} - \text{Observed Hb}) \times \text{LBW} + (0.26 \times \text{LBW})$$

Desired Hb = the target hemoglobin in g/dL

Observed Hb = the patient's current hemoglobin in g/dL

LBW = Lean body weight in kg [Males: LBW = 50 kg + 2.4 kg for each inch of patient's height over 5 feet; Females: LBW = 45.5 kg + 2.3 kg for each inch of patient's height over 5 feet.]

The following formula can be utilized to calculate the total dose for children 5 to 15 kg:

$$\text{Dose (mL)} = 0.0442 (\text{Desired Hb} - \text{Observed Hb}) \times \text{W} + (0.26 \times \text{W})$$

Desired Hb = the target hemoglobin in g/dL

W = body weight in kg

No more than 2 mL of INFed should be administered per day. Daily doses should be given until the total required dose is administered.

The recommended dosage for blood loss is based on the approximate amount of blood loss and pretreatment hematocrit.

$$\text{Dose (mL)} = [\text{Blood loss (in mL)} \times \text{hematocrit}] \div 50 \text{ mg/mL}$$

Injectafer (ferric carboxymaltose): Available as 100 mg/2 mL, 750 mg/15 mL, and 1,000 mg/20 mL single-dose vials. The recommended dosage for iron deficiency anemia in patients weighing 50 kg or

more is 750 mg in two doses separated by at least 7 days for a total of 1,500 mg per course. For adults, a single dose of 15 mg/kg up to a maximum dose of 1,000 mg may be administered as an alternative. Persons weighing less than 50 kg should receive 15 mg/kg in two doses separated by at least 7 days per course. In patients with heart failure, this dose is modified based on weight and hemoglobin (g/dL). Additional maintenance doses of 500 mg at 12, 24, and 36 weeks is recommended for heart failure patients with a serum ferritin less than 100 ng/mL or between 100-300 ng/mL with a transferrin saturation less than 20%. Injectafer treatment can be repeated if iron deficiency reoccurs.

Monoferic (ferric derisomaltose): Available in 100 mg/mL, 500 mg/5 mL, and 1,000 mg/10 mL single-dose vials. The recommended dose for patients weighing 50 kg or more is 1,000 mg. The recommended dose for patients weighing less than 50 kg is 20 mg/kg. Repeat treatment if iron deficiency anemia reoccurs.

Venofer (iron sucrose): Available as 50 mg/2.5 mL, 100 mg/5 mL, and 200 mg/10 mL in single-dose vials. The recommended dose is based on the patient's age and diagnosis.

- Adult hemodialysis dependent chronic kidney disease (HDD-CKD): 100 mg per infusion for a total treatment course of 1,000 mg.
- Adult non-dialysis dependent chronic kidney disease (NDD-CKD): 200 mg per infusion.
- Adult peritoneal dialysis dependent chronic kidney disease (PDD-CKD): 300 mg or 400 mg per infusion.
- Pediatric HDD-CKD maintenance treatment: 0.5 mg/kg, not to exceed 100 mg per dose, every 2 weeks for 12 weeks total.
- Pediatric PDD-CKD or NDD-CKD who are on erythropoietin therapy: 0.5 mg/kg, not to exceed 100 mg per dose, every 4 weeks for 12 weeks.

COVERAGE

The OSU Health Plan considers intravenous iron therapy medically necessary for covered persons with iron deficiency or iron deficiency anemia who meet all of the following criteria:

- Presence of one or more of the following indications:
 - Cancer- and chemotherapy-induced anemia; or
 - Chronic kidney disease (CKD); or

- Congestive heart failure (CHF); or
- Contraindication to oral iron; or
- Inflammatory bowel disease (ulcerative colitis or Crohn's disease); or
- Failure of a 4-week trial of oral iron; or
- Gastric surgery (bypass or resection); or
- Malabsorption syndrome (celiac disease, Whipple's disease); or
- Ongoing blood loss that exceeds the capacity of oral iron to meet needs (e.g., heavy uterine bleeding); or
- Restless leg syndrome (RLS) and one or more of the following:
 - Malabsorption state
 - Intolerance to oral preparations
 - Moderate to severe symptoms despite trial of oral iron
- Unable to tolerate oral iron (Side effects must be documented by a physician and be severe in nature despite conservative interventions to manage symptoms. For example, constipation must persist despite an appropriate trial of stool softeners.); or
- Women in the second or third trimester who cannot tolerate oral iron or whose anemia did not improve with oral iron; or
- Women in the third trimester for whom there would be insufficient time to replete iron orally (after week 30)
- Laboratory values obtained within the last 30 days confirm diagnosis of iron deficiency:
 - Acute or chronic inflammatory condition:
 - Serum ferritin < 100 ng/ml; or
 - Transferrin saturation < 20%
 - Anemia from cancer or chemotherapy:
 - Serum ferritin < 30 ng/ml and transferrin saturation < 20%; or
 - Serum ferritin < 500 ng/ml and transferrin saturation < 50% in patients receiving an erythropoiesis-stimulating agent (ESA); or
 - Serum ferritin > 500 ng/mL and transferrin saturation < 50%

- Chronic kidney disease (dialysis):
 - Serum ferritin \leq 200 ng/ml and transferrin saturation \leq 20%; or
 - Serum ferritin $<$ 500 ng/ml, transferrin saturation \leq 30%, and one or more of the following:
 - Hemoglobin $<$ 10 g/dl; or
 - Patient is receiving an erythropoiesis-stimulating agent (ESA)
- Chronic kidney disease (without dialysis):
 - Serum ferritin $<$ 100 ng/ml; or
 - Transferrin saturation $<$ 20%
- Patients without chronic kidney disease or other comorbid condition:
 - Serum ferritin $<$ 30 ng/ml; or
 - Transferrin saturation $<$ 20%
- Pregnancy:
 - Serum ferritin $<$ 30 ng/mL; or
 - Transferrin saturation $<$ 20%
- Restless leg syndrome (RLS):
 - Serum ferritin \leq 100 ng/ml and transferrin saturation $<$ 45%

EXCLUSIONS

Intravenous iron is contraindicated for patients with a history of an allergic reaction to any intravenous iron product.

There is a greater risk of anaphylaxis in patients with multiple drug allergies.

OSU Health Plan considers intravenous iron therapy experimental and investigational for all other indications including the following (not an all-inclusive list) because its clinical value for these indications has not been established:

- Acute mountain sickness
- Prophylactic use to improve function in non-anemic persons undergoing surgery for hip fracture

- Prophylactic use to prevent postoperative anemia in persons undergoing bariatric surgery
- Empiric treatment of restless legs syndrome when above criteria are not met
- Treatment of post-operative anemia following major surgery (e.g., cardiothoracic surgery, colorectal cancer surgery, and neurosurgery)
- Pre-operative intravenous iron therapy for reduction of transfusions during major surgery
- Use in the first trimester of pregnancy
- Infertility
- Prior to in vitro fertilization (IVF)
- Genetic hemochromatosis or hemochromatosis secondary to iron overload

Intravenous iron therapy for athletic performance is excluded from coverage according to the OSU Specific Plan Details (SPD).

PRIOR AUTHORIZATION

Prior authorization is required for intravenous iron therapy. Refer to the Prior Authorization Guide at www.osuhealthplan.com.

CODES

Code	Description
J1437	Injection, ferric derisomaltose, 10 mg
J1439	Injection, ferric carboxymaltose, 1 mg
J1443	Injection, ferric pyrophosphate citrate solution, 0.1 mg of iron
J1444	Injection, ferric pyrophosphate citrate powder, 0.1 mg of iron
J1445	Injection, ferric pyrophosphate citrate solution (Triferic AVNU), 0.1 mg of iron
J1750	Injection, iron dextran, 50 mg
J1756	Injection, iron sucrose, 1 mg
J2916	Injection, sodium ferric gluconate complex in sucrose injection, 12.5 mg
Q0138	Injection, ferumoxytol, for treatment of iron deficiency anemia, 1 mg (non-ESRD use)

Q0139	Injection, ferumoxytol, for treatment of iron deficiency anemia, 1 mg (for ESRD on dialysis)
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REFERENCES

- Aetna. (2024). Intravenous Iron Therapy. Retrieved from http://www.aetna.com/cpb/medical/data/500_599/0575.html.
- Albaramki J, Hodson EM, Craig JC, Webster AC. Parenteral versus oral iron therapy for adults and children with chronic kidney disease. Cochrane Database of Systematic Reviews 2012, Issue 1. Art. No.: CD007857. DOI: 10.1002/14651858.CD007857.pub2
- AMAG Pharmaceuticals, Inc. (2015, March). Feraheme. Retrieved March 11, 2016, from http://www.feraheme.com/pdfs/Feraheme_Full_Prescribing_Information_2015.pdf
- American College of Obstetricians and Gynecologists (ACOG). Anemia in pregnancy. ACOG Practice Bulletin No. 95. Washington, DC: ACOG; July 2005.
- Auerbach, M. (2021, November 1). Causes and diagnosis of iron deficiency and iron deficiency anemia in adults (W.C. Mentzer, R.T. Means, J.G. Elmore, J.S. Tirnauer, & L. Kunins, Eds.). https://www.uptodate.com/contents/causes-and-diagnosis-of-iron-deficiency-and-iron-deficiency-anemia-in-adults?search=iron%20deficiency&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1#H44
- Auerbach, M. (2022, January 26). Treatment of iron deficiency anemia in adults (W.C. Mentzer, R.T. Means, J.S. Tirnauer, & L. Kunins, Eds.). https://www.uptodate.com/contents/treatment-of-iron-deficiency-anemia-in-adults?search=iron%20deficiency&source=search_result&selectedTitle=2~150&usage_type=default&display_rank=2#H220570
- Auerbach, M., & Landy, H.J. (2024). Anemia in pregnancy (L.L. Simpson, R.T. Means, J.S. Tirnauer, & V.A. Barss, Eds.). https://www.uptodate.com/contents/anemia-in-pregnancy?search=anemia%20in%20pregnancy&source=search_result&selectedTitle=1%7E150&usage_type=default&display_rank=1#H3811955054
- Braunstein, E.M. (2018). Iron deficiency anemia. Merck Manual. Retrieved from <https://www.merckmanuals.com/professional/hematology-and-oncology/anemias-caused-by-deficient-erythropoiesis/iron-deficiency-anemia#v969223>

CGS Administrators. (2016). Iron sucrose, iron dextran and ferumoxytol, (Intravenous iron therapy).

Local Coverage Article. Retrieved from <https://www.cms.gov/medicare-coverage-database/details/article-details.aspx?articleId=52427&ver=12&SearchType=Advanced&CoverageSelection=Both&NCElection=NCA%7cCAL%7cNCD%7cMEDCAC%7cTA%7cMCD&ArticleType=SAD%7cEd&PolicyType=Both&s=All&Keyword=iron&KeywordLookUp=Doc&KeywordSearchType=Exact&kq=true&bc=IAAAACAAAA&>

"Faculty and Staff Health Plans Specific Plan Details Document." The Ohio State University Office of Human Resources, 31 Dec. 2018. Web. <https://hr.osu.edu/wp-content/uploads/medical-sp.pdf>

Gordon M, Sinopoulou V, Ihezor-Ejiofor Z, Iqbal T, Allen P, Hoque S, Engineer J, Akobeng AK.

Interventions for treating iron deficiency anaemia in inflammatory bowel disease. *Cochrane Database of Systematic Reviews* 2021, Issue 1. Art. No.: CD013529. DOI: 10.1002/14651858.CD013529.pub2

Gurusamy K, Nagendran M, Broadhurst JF, Anker SD, Richards T. Iron therapy in anaemic adults without chronic kidney disease. *Cochrane Database of Systematic Reviews* 2014, Issue 12. Art. No.: CD010640. DOI: 10.1002/14651858.CD010640.pub2

Hetzel, D., Strauss, W., Bernard, K., Li, Z., Urboniene, A., & Allen, L.F. (June 2014). A phase III, randomized, open-label trial of ferumoxytol compared with iron sucrose for the treatment of iron deficiency anemia in patients with a history of unsatisfactory oral iron therapy. *American Journal of Hematology*, 89(6), 646-650

Landry, R., Jacobs, P. M., Davis, R., Shenouda, M., & Bolton, W. K. (2005). Pharmacokinetic study of ferumoxytol: A new iron replacement therapy in normal subjects and hemodialysis patients. *American Journal of Nephrology*, 25, 400-410.

Markova V, Norgaard A, Jørgensen K, Langhoff-Roos J. Treatment for women with postpartum iron deficiency anaemia. *Cochrane Database of Systematic Reviews* 2015, Issue 8. Art. No.: CD010861. DOI: 10.1002/14651858.CD010861.pub2

McCormack, P. L. (2012). Ferumoxytol in iron deficiency anaemia in adults with chronic kidney disease. *Adis Drug Profile*, 72(15), 2013-2022.

Mechanick JI, Youdim A, Jones DB, et al; American Association of Clinical Endocrinologists, Obesity Society, American Society for Metabolic & Bariatric Surgery. Clinical practice guidelines for the perioperative nutritional, metabolic, and nonsurgical support of the bariatric surgery patient -- 2013 update: Cosponsored by American Association of Clinical Endocrinologists, the Obesity

Society, and American Society for Metabolic & Bariatric Surgery. *Endocr Pract.* 2013;19(2):337-372.

Mhaskar R, Wao H, Miladinovic B, Kumar A, Djulbegovic B. The role of iron in the management of chemotherapy-induced anemia in cancer patients receiving erythropoiesis-stimulating agents. *Cochrane Database of Systematic Reviews* 2016, Issue 2. Art. No.: CD009624. DOI: 10.1002/14651858.CD009624.pub2

Miles LF, Litton E, Imberger G, Story D. Intravenous iron therapy for non-anaemic, iron-deficient adults. *Cochrane Database of Systematic Reviews* 2019, Issue 12. Art. No.: CD013084. DOI: 10.1002/14651858.CD013084.pub2

National Kidney Foundation (NKF). NKF-K/DOQI Clinical Practice Guidelines for Anemia of Chronic Kidney Disease: Update 2000. New York, NY: NKF; 2000.

Ng O, Keeler BD, Mishra A, Simpson A, Neal K, Brookes MJ, Acheson AG. Iron therapy for pre-operative anaemia. *Cochrane Database of Systematic Reviews* 2015, Issue 12. Art. No.: CD011588. DOI: 10.1002/14651858.CD011588.pub2

O'Lone EL, Hodson EM, Nistor I, Bolignano D, Webster AC, Craig JC. Parenteral versus oral iron therapy for adults and children with chronic kidney disease. *Cochrane Database of Systematic Reviews* 2019, Issue 2. Art. No.: CD007857. DOI: 10.1002/14651858.CD007857.pub3

Revez L, Gyte GML, Cuervo LG, Casasbuenas A. Treatments for iron-deficiency anaemia in pregnancy. *Cochrane Database of Systematic Reviews* 2011, Issue 10. Art. No.: CD003094. DOI: 10.1002/14651858.CD003094.pub3

Schrier, S. L., & Auerbach, M. (2016, February 11). Treatment of iron deficiency anemia in adults.

Retrieved March 11, 2016, from http://www.uptodate.com/contents/treatment-of-iron-deficiency-anemia-in-adults?source=search_result&search=iron+deficiency+anemia&selectedTitle=2~150

Silber, M. H. (2020, November 18). Treatment of restless legs syndrome and periodic limb movement disorder in adults (H. I. Hurtig, A. Y. Avidan, & A. F. Elchler, Eds.). Retrieved February 18, 2021, from https://www.uptodate.com/contents/treatment-of-restless-legs-syndrome-and-periodic-limb-movement-disorder-in-adults?search=restless%20leg%20syndrome&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1#H1663765

Silber, M. H. (2022, January 19). Management of restless legs syndrome and periodic limb movement disorder in adults (H.I. Hurtig, A.Y. Avidan, & A.F. Elchler, Eds.).

https://www.uptodate.com/contents/management-of-restless-legs-syndrome-and-periodic-limb-movement-disorder-in-adults?search=restless%20leg%20syndrome&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1#H1663765

Trotti LM, Bhadriraju S, Becker LA. Iron for restless legs syndrome. Cochrane Database of Systematic Reviews 2012, Issue 5. Art. No.: CD007834. DOI: 10.1002/14651858.CD007834.pub2

Winkelman, J. W., et al. (2016). Practice guideline summary: Treatment of restless legs syndrome in adults. Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. *Neurology*, 87, 2585-2593.