THE OHIO STATE UNIVERSITY
HEALTH PLAN

Subject: Intravenous Iron Therapy

Effective Date: 4/2016
Revision Date: 4/2022

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:

- Dexferrum (iron dextran)
- Injectafer (ferric carboxymaltose)
- Feraheme (ferumoxytol)
- Ferrlecit / Nulecit (sodium ferric gluconate complex)
- Venofer (iron sucrose)

COVERAGE

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

- Presence of one or more of the following indications:
    - Inflammatory bowel disease (ulcerative colitis or Crohn's disease); or
    - Gastric surgery (bypass or resection); or
    - Chronic kidney disease (CKD); or
    - Cancer diagnosis who are receiving an erythropoiesis-stimulating agent (ESA); or
    - Unable to tolerate oral iron (side effects must be documented by a physician and be severe in nature); or
    - Ongoing blood loss that exceeds the capacity of oral iron to meet needs (e.g., heavy uterine bleeding); or
    - Malabsorption syndrome (celiac disease, Whipple's disease); or
    - Congestive heart failure (CHF); or
    - Women in the second or third trimester who cannot tolerate oral iron or whose anemia did not improve with oral iron; 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
- Laboratory values obtained within the last 30 days confirm diagnosis of iron deficiency:
    - Patients without chronic kidney disease or other comorbid condition identified below:
        - Serum ferritin < 30 ng/ml; or
        - Transferrin saturation < 20%

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

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

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, 1mg
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)

REFERENCES

Aetna. (2021). 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

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&NCSelection=NCA%7cCAL%7cNCD%7cMEDCAC%7cTA%7cMCD&ArticleType=SAD%7cEd&PolicyType=Both&s=All&KeyWord=iron&KeyWordLookUp=Doc&KeyWordSearchType=Exact&kq=true&bc=IAAAACAAAAAA&

"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-spd.pdf

Gordon M, Sinopoulou V, Iheozor-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). Pharmacokinectic 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

Reveiz 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.