Oscar Clinical Guideline: Injectable Iron Supplements (PG196, Ver. 4)

Injectable Iron Supplements

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

Summary

Iron deficiency anemia (IDA) is a condition characterized by insufficient iron levels in the body, resulting in decreased production of healthy red blood cells. Iron is crucial for the synthesis of hemoglobin, a protein responsible for transporting oxygen to tissues. Symptoms of iron deficiency anemia include fatigue, weakness, pale skin, shortness of breath, dizziness, and cold hands and feet. In the United States, IDA is the most common cause of anemia, and it disproportionately affects menstruating and pregnant individuals, older adults (defined as those 65 years of age and older), and Black, Native and Hispanic Americans.

Causes of iron deficiency anemia include inadequate dietary iron intake, poor iron absorption, increased iron requirements (e.g., during pregnancy), and chronic blood loss. Treatment typically involves oral iron

supplementation to replenish iron stores. In severe cases or when oral supplements are ineffective, injectable iron or blood transfusions may be necessary. Injectable iron supplements, including sodium ferric gluconate, ferric carboxymaltose, ferumoxytol, iron dextran, and ferric derisomaltose, are used to treat iron deficiency anemia (IDA) in patients who cannot tolerate or have an inadequate response to oral iron therapy. Additionally, certain injectable iron supplements may also be used to treat iron deficiency in heart failure with reduced ejection fraction or restless legs syndrome (RLS) with moderate to severe symptoms and low iron levels.

NOTE: The Plan also has a Medical Benefit Preferred Physician-Administered Drug Exceptions Criteria policy (Clinical Guideline CG107) that outlines the preferred and non-preferred injectable iron products, and the exception criteria required for coverage of non-preferred products.

Definitions

"Anemia" refers to a condition in which the body lacks sufficient healthy red blood cells to carry adequate oxygen to the body's tissues. It can be caused by various factors, including iron deficiency.

"Chronic kidney disease" is a condition characterized by gradual loss of kidney function over time.

"Erythropoiesis-stimulating agents (ESAs)" are medications that stimulate the bone marrow to produce more red blood cells. They are sometimes used in conjunction with iron therapy to treat anemia in certain conditions, such as chronic kidney disease.

"Hemoglobin" refers to a protein responsible for transporting oxygen to tissues.

"Iron deficiency anemia (IDA)" refers to a condition characterized by insufficient iron levels in the body, resulting in decreased production of healthy red blood cells.

"Iron overload" or "hemochromatosis" refers to a condition characterized by excessive iron accumulation in the body.

"Malabsorption condition" refers to a condition that prevents adequate absorption of nutrients, including iron, from the intestines (e.g., inflammatory bowel disease, celiac disease, bariatric surgery).

"Menorrhagia" refers to abnormally heavy or prolonged menstrual bleeding, which can lead to iron deficiency anemia.

"Oral iron supplementation" refers to the use of iron supplements taken by mouth, usually in the form of tablets, capsules, or liquid preparations.

"Parenteral iron" or "injectable iron" refers to iron supplementation administered through intravenous (IV) or intramuscular (IM) routes.

"Restless legs syndrome (RLS)" or "Willis-Ekbom disease" is a neurological disorder characterized by an uncontrollable urge to move the legs, often accompanied by uncomfortable sensations. It can be associated with iron deficiency in some cases.

"Serum ferritin" is a laboratory test that measures the amount of iron stored in the body.

"Transferrin saturation (TSAT)" refers to a laboratory test that measures the percentage of transferrin (a protein that transports iron) that is saturated with iron.

Medical Necessity Criteria for Initial Authorization

Iron Deficiency Anemia (IDA) or Iron Deficiency Without Anemia

The Plan considers injectable iron supplements medically necessary when ALL of the following criteria are met:

1. The member has a diagnosis of iron deficiency anemia (IDA) OR iron deficiency without anemia confirmed by recent (within the last 90 days) laboratory results showing ALL of the following:
    a. ONE of the following:
        i. Hemoglobin less than 12.5 g/dL in females; *or*
        ii. Hemoglobin less than 13.5 g/dL in males; *or*
        iii. Evidence of symptomatic iron deficiency without anemia (e.g., fatigue, weakness, shortness of breath, pica); *and*
    b. ONE of the following:
        i. Serum ferritin less than or equal to (≤) 30 ng/mL; *or*
        ii. Serum ferritin ≤ 100 ng/mL with transferrin saturation (TSAT) ≤ 20%; *or*
        iii. For iron deficiency in the presence of inflammatory conditions (*acute or chronic*), malignancy, or other complicating factors (*e.g., recent blood transfusion or IV iron administration within 4-6 weeks*), ANY of the following:
            1. serum ferritin ≤ 100 ng/mL, regardless of TSAT; *and/or*
            2. serum ferritin 100-300 ng/mL with TSAT < 20% and ONE of the following:
                a. elevated inflammatory markers (e.g., C-reactive protein, ESR); *or*
                b. Presence of a chronic inflammatory condition (e.g., RA, IBD); *or*
                c. Presence of a malignancy; *or*
                d. Clinical signs and symptoms strongly suggestive of iron deficiency; *and/or*
            3. Clinical evidence of iron deficiency in the context of a condition known to elevate ferritin (e.g., acute inflammation, alcohol-related liver disease,

anemia of chronic disease, idiopathic pulmonary hemosiderosis) or affect TSAT (e.g., recent transfusion or IV iron administration within 12-weeks); *or*

iv. TSAT < 20% in the presence of condition(s) affecting iron utilization or metabolism, such as:
    1. Chronic kidney disease (CKD) stages 3-5 or end-stage renal disease (ESRD) on dialysis; *or*
    2. Use of Erythropoiesis-stimulating agents (ESAs) for anemia related to CKD or cancer; *or*
    3. Chronic inflammation with ferritin levels > 300 ng/mL; *AND*

2. The member has ONE or more of the following clinical scenarios:
    a. Chronic kidney disease (with or without hemodialysis); *and/or*
    b. Documented intolerance, contraindication, or inadequate response after a 1-month trial of oral iron therapy taken at least every other day; *and/or*
    c. ANY condition requiring rapid iron repletion, such as:
        i. Severe anemia (Hb < 8 g/dL) OR requiring blood transfusions; *or*
        ii. Anticipated excessive blood loss from planned surgery; *or*
        iii. Severe menorrhagia/abnormal uterine bleeding; *or*
        iv. Severe ongoing blood loss (e.g., varices); *or*
        v. Second or third trimester pregnancy with hemoglobin <10.5 g/dL; *or*
        vi. Chemotherapy-induced iron deficiency without response to oral iron trial; *and/or*
    d. Malabsorption condition likely to prevent adequate oral iron absorption (e.g. inflammatory bowel disease, celiac disease,whipple's disease, autoimmune gastritis, bariatric surgery); *AND*
3. The member has no evidence of a history of hypersensitivity to the requested iron product or any component of the formulation; *AND*
4. The requested product is being prescribed at a dose and frequency that is within FDA approved labeling OR is supported by compendia or evidence-based published dosing guidelines for the requested indication.

<u>Iron Deficiency in Heart Failure</u>

The Plan considers <u>Injectafer (ferric carboxymaltose)</u> medically necessary when ALL of the following criteria are met:

1. The member is 18 years of age or older; *AND*
2. The member has a diagnosis of iron deficiency AND documentation of ALL of the following:
    a. Heart failure with reduced ejection fraction (HFrEF), defined as left ventricular ejection fraction (LVEF) ≤ 45%; *and*
    b. Recent (within the last 90 days) serum ferritin < 100 ng/mL or 100-300 ng/mL with TSAT < 20%; *AND*

3. The member has no evidence of a history of hypersensitivity to ferric carboxymaltose or any of its components; *AND*
4. Injectafer (ferric carboxymaltose) is being prescribed at a dose and frequency that is within FDA approved labeling OR is supported by compendia or evidence-based published dosing guidelines for the requested indication.

Restless Legs Syndrome (RLS)/Willis-Ekbom Disease

The Plan considers INFeD (iron dextran complex) or Injectafer (ferric carboxymaltose) medically necessary when ALL of the following criteria are met:

1. The member is 18 years of age or older; *AND*
2. The member has a diagnosis of RLS or Willis-Ekbom disease with:
    a. Moderate to severe symptoms; *and*
    b. Recent (within the last 90 days) serum ferritin ≤ 100 mcg/L with TSAT < 45%; *AND*
3. The member has documented intolerance, contraindication, or inadequate response after a 1-month trial of oral iron supplementation; *AND*
4. The member meets ALL of the following:
    a. No evidence of serum ferritin levels greater than 300 ng/mL OR TSAT greater than 45%; *or*
    b. No evidence of a history of hypersensitivity to the requested iron product or any of its components; *AND*
5. The requested product is being prescribed at a dose and frequency that is within FDA approved labeling OR is supported by compendia or evidence-based published dosing guidelines for RLS.

If the above prior authorization criteria are met, the requested product will be authorized for up to 90-days.

Medical Necessity Criteria for Reauthorization

Iron deficiency anemia (IDA) or Iron Deficiency Without Anemia

Reauthorization for up to 3-months will be granted if the member has recent (within the last 30-days) clinical chart documentation demonstrating ALL of the following criteria:

1. The member continues to meet applicable Initial Authorization criteria and requires additional iron repletion; *AND*
2. Documentation of clinical response from prior iron treatment, as evidenced by one or more of the following:
    a. Improved hemoglobin ≥ 1-2 g/dL or hematocrit ≥ 3-6% from baseline; *and/or*
    b. Improvement in iron deficiency signs/symptoms (e.g. fatigue, weakness, shortness of breath, pica); *and/or*
    c. Reduced ESA dose or transfusion requirements; *AND*

3. Current serum ferritin ≤ 300 ng/mL and TSAT ≤ 50% (unless adequately explained by concomitant condition); *AND*
4. There is no evidence of serious toxicity or hypersensitivity from the drug.

Iron Deficiency in Heart Failure

Reauthorization for up to 3-months will be granted if the member has recent (within the last 30-days) clinical chart documentation demonstrating ALL of the following criteria:

1. The member continues to meet applicable Initial Authorization criteria; *AND*
2. Documentation of clinical response from prior iron treatment, as evidenced by one or more of the following:
    a. Improvement in heart failure symptoms or functional capacity; *and/or*
    b. Reduced hospitalizations for heart failure; *AND*
3. Current serum ferritin < 100 ng/mL or 100-300 ng/mL with TSAT < 20%; *AND*
4. There is no evidence of serious toxicity or hypersensitivity from the drug.

Restless Legs Syndrome (RLS)/Willis-Ekbom Disease

Reauthorization for up to 3-months will be granted if the member has recent (within the last 30-days) clinical chart documentation demonstrating ALL of the following criteria:

1. The member continues to meet applicable Initial Authorization criteria and has persistent RLS symptoms requiring additional iron repletion; *AND*
2. Documentation of clinical response from prior iron treatment, as evidenced by improvement in RLS symptom severity or frequency; *AND*
3. Current serum ferritin ≤ 100 mcg/L with TSAT < 45%; *AND*
4. There is no evidence of serious toxicity or hypersensitivity from the drug.

Experimental or Investigational / Not Medically Necessary

Injectable Iron Supplements for any indication or use not listed in the Medical Necessity Criteria above are considered experimental, investigational, or not medically necessary by the Plan. This includes, but is not limited to, the following:

- Acute mountain sickness.
- Non-anemic conditions:
    - To improve exercise performance or functional capacity in non-iron deficient individuals.
    - For prophylactic use prior to orthopedic or other surgical procedures in non-iron deficient patients.
- Any other indication not supported by major compendia or evidence-based clinical practice guidelines.
- The use of injectable iron is considered not medically necessary in the following circumstances:
    - Documented iron overload or hemochromatosis.

- Serum ferritin levels > 500 ng/mL, unless adequately explained by a concomitant condition.
- TSAT > 50%, unless adequately explained by a concomitant condition.
- Pre-operative use solely to reduce/avoid transfusion needs for non-anemic, non-iron deficient surgical patients, including those with belief systems that preclude the use of blood transfusions.
- Continued use when there is no evidence of clinical response after an adequate trial of injectable iron therapy.

Applicable Billing Codes (HCPCS/CPT Codes)

Table 1:	
CPT/HCPCS Codes considered Iron Deficiency Anemia and Iron Deficiency Without Anemia considered medically necessary if criteria are met:	
Code	*Description*
J1437	Monoferric Injection, ferric derisomaltose, 10 mg
J1439	Injectafer Injection, ferric carboxymaltose, 1 mg
J1750	Infed Injection, iron dextran, 50 mg
J1756	Venofer Injection, iron sucrose, 1 mg
J2916	Ferrlecit Injection, sodium ferric gluconate complex in sucrose injection, 12.5 mg
Q0138	Feraheme Injection, ferumoxytol, for treatment of iron deficiency anemia, 1 mg (non-esrd use)
Q0139	Feraheme Injection, ferumoxytol, for treatment of iron deficiency anemia, 1 mg (for esrd on dialysis)

Table 2:

ICD-10 diagnosis codes considered medically necessary for Iron Deficiency Anemia and Iron Deficiency Without Anemia with Table 1 (CPT/HCPCS) if criteria are met:	
Code	*Description*
D50.0	Iron deficiency anemia secondary to blood loss (chronic)
D50.1	Sideropenic dysphagia
D50.8	Other iron deficiency anemias
D50.9	Iron deficiency anemia, unspecified
D55.21	Anemia due to pyruvate kinase deficiency
D55.29	Anemia due to other disorders of glycolytic enzymes
D59.10	Autoimmune hemolytic anemia, unspecified
D59.11	Warm autoimmune hemolytic anemia
D59.12	Cold autoimmune hemolytic anemia
D59.13	Mixed type autoimmune hemolytic anemia
D59.19	Other autoimmune hemolytic anemia
D62	Acute posthemorrhagic anemia
D63.0	Anemia in neoplastic disease
D63.1	Anemia in chronic kidney disease
D63.8	Anemia in other chronic diseases classified elsewhere
D64.81	Anemia due to antineoplastic chemotherapy
D64.89	Other specified anemias
D64.9	Anemia, unspecified
K50.0	Crohn's disease of small intestine
K50.00	Crohn's disease of small intestine without complications
K50.01	Crohn's disease of small intestine with complications
K50.011	Crohn's disease of small intestine with rectal bleeding
K50.012	Crohn's disease of small intestine with intestinal obstruction
K50.013	Crohn's disease of small intestine with fistula
K50.014	Crohn's disease of small intestine with abscess
K50.018	Crohn's disease of small intestine with other complication
K50.019	Crohn's disease of small intestine with unspecified complications
K50.1	Crohn's disease of large intestine
K50.10	Crohn's disease of large intestine without complications
K50.11	Crohn's disease of large intestine with complications
K50.111	Crohn's disease of large intestine with rectal bleeding

K50.112	Crohn's disease of large intestine with intestinal obstruction
K50.113	Crohn's disease of large intestine with fistula
K50.114	Crohn's disease of large intestine with abscess
K50.118	Crohn's disease of large intestine with other complication
K50.119	Crohn's disease of large intestine with unspecified complications
K50.8	Crohn's disease of both small and large intestine
K50.80	Crohn's disease of both small and large intestine without complications
K50.81	Crohn's disease of both small and large intestine with complications
K50.811	Crohn's disease of both small and large intestine with rectal bleeding
K50.812	Crohn's disease of both small and large intestine with intestinal obstruction
K50.813	Crohn's disease of both small and large intestine with fistula
K50.814	Crohn's disease of both small and large intestine with abscess
K50.818	Crohn's disease of both small and large intestine with other complication
K50.819	Crohn's disease of both small and large intestine with unspecified complications
K50.9	Crohn's disease, unspecified
K50.90	Crohn's disease, unspecified, without complications
K50.91	Crohn's disease, unspecified, with complications
K50.911	Crohn's disease, unspecified, with rectal bleeding
K50.912	Crohn's disease, unspecified, with intestinal obstruction
K50.913	Crohn's disease, unspecified, with fistula
K50.914	Crohn's disease, unspecified, with abscess
K50.918	Crohn's disease, unspecified, with other complication
K50.919	Crohn's disease, unspecified, with unspecified complications
K90.0	Celiac disease
K90.1	Tropical sprue
K90.2	Blind loop syndrome, not elsewhere classified
K90.3	Pancreatic steatorrhea
K90.4	Other malabsorption due to intolerance
K90.41	Non-celiac gluten sensitivity
K90.49	Malabsorption due to intolerance, not elsewhere classified
K90.8	Other intestinal malabsorption
K90.81	Whipple's disease
K90.82	Short bowel syndrome
K90.821	Short bowel syndrome with colon in continuity

K90.822	Short bowel syndrome without colon in continuity
K90.829	Short bowel syndrome, unspecified
K90.83	Intestinal failure
K90.89	Other intestinal malabsorption
K90.9	Intestinal malabsorption, unspecified
N18.1	Chronic kidney disease, stage 1
N18.2	Chronic kidney disease, stage 2 (mild)
N18.3	Chronic kidney disease, stage 3 (moderate)
N18.30	Chronic kidney disease, stage 3 unspecified
N18.31	Chronic kidney disease, stage 3a
N18.32	Chronic kidney disease, stage 3b
N18.4	Chronic kidney disease, stage 4 (severe)
N18.5	Chronic kidney disease, stage 5
N18.6	End stage renal disease
O99.01	Anemia complicating pregnancy
O99.011	Anemia complicating pregnancy, first trimester
O99.012	Anemia complicating pregnancy, second trimester
O99.013	Anemia complicating pregnancy, third trimester
O99.019	Anemia complicating pregnancy, unspecified trimester
P61.2	Anemia of prematurity
T88.8XXA	Other specified complications of surgical and medical care, not elsewhere classified, initial encounter
T88.8XXD	Other specified complications of surgical and medical care, not elsewhere classified, subsequent encounter

Table 3:	
CPT/HCPCS Codes for Iron Deficiency in Heart Failure considered medically necessary if criteria are met:	
Code	*Description*
J1439	Injectafer Injection, ferric carboxymaltose, 1 mg

Table 4:	
ICD-10 diagnosis codes considered medically necessary for Iron Deficiency in Heart failure with Table 3 (CPT/HCPCS) if criteria are met:	
Code	*Description*
I09.81	Rheumatic heart failure
I11.0	Hypertensive heart disease with heart failure
I50.0	Heart failure
I50.1	Left ventricular failure, unspecified
I50.2	Systolic (congestive) heart failure
I50.20	Unspecified systolic (congestive) heart failure
I50.21	Acute systolic (congestive) heart failure
I50.22	Chronic systolic (congestive) heart failure
I50.23	Acute on chronic systolic (congestive) heart failure
I50.3	Diastolic (congestive) heart failure
I50.30	Unspecified diastolic (congestive) heart failure
I50.31	Acute diastolic (congestive) heart failure
I50.32	Chronic diastolic (congestive) heart failure
I50.33	Acute on chronic diastolic (congestive) heart failure
I50.4	Combined systolic (congestive) and diastolic (congestive) heart failure
I50.40	Unspecified combined systolic (congestive) and diastolic (congestive) heart failure
I50.41	Acute combined systolic (congestive) and diastolic (congestive) heart failure
I50.42	Chronic combined systolic (congestive) and diastolic (congestive) heart failure
I50.43	Acute on chronic combined systolic (congestive) and diastolic (congestive) heart failure
I50.8	Other heart failure
I50.81	Right heart failure
I50.810	Right heart failure, unspecified
I50.811	Acute right heart failure

I50.812	Chronic right heart failure
I50.813	Acute on chronic right heart failure
I50.814	Right heart failure due to left heart failure
I50.82	Biventricular heart failure
I50.83	High output heart failure
I50.84	End stage heart failure
I50.89	Other heart failure
I50.9	Heart failure, unspecified

Table 5:	
CPT/HCPCS Codes for Restless Legs Syndrome (RLS)/Willis-Ekbom Disease considered medically necessary if criteria are met:	
Code	*Description*
J1439	Injectafer Injection, ferric carboxymaltose, 1 mg
J1750	Infed Injection, iron dextran, 50 mg

Table 6:	
ICD-10 diagnosis codes considered medically necessary for Restless Legs Syndrome (RLS)/Willis-Ekbom Disease with Table 5 (CPT/HCPCS) if criteria are met:	
Code	*Description*
G25.81	Restless legs syndrome

References

1. Allen RP, Picchietti DL, Auerbach M, et al; International Restless Legs Syndrome Study Group (IRLSSG). Evidence-based and consensus clinical practice guidelines for the iron treatment of restless legs syndrome/Willis-Ekbom disease in adults and children: an IRLSSG task force report. Sleep Med. 2018;41:27-44. doi:10.1016/j.sleep.2017.11.1126
2. American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Obstetrics. ACOG Practice Bulletin No. 233: Anemia in pregnancy. Obstet Gynecol. 2021;138(2):e55-e64. doi:10.1097/AOG.0000000000004477

3. Anemia in Pregnancy: ACOG Practice Bulletin, Number 233. Obstet Gynecol. 2021 Aug 1;138(2):e55-e64. doi: 10.1097/AOG.0000000000004477. PMID: 34293770.
4. Anker SD, Comin Colet J, Filippatos G, et al. Ferric carboxymaltose in patients with heart failure and iron deficiency. N Engl J Med. 2009 Dec 17;361(25):2436-48. doi: 10.1056/NEJMoa0908355. Epub 2009 Nov 17.
5. Anker SD, Friede T, Butler J, et al. Intravenous Ferric Carboxymaltose in Heart Failure With Iron Deficiency: The FAIR-HF2 DZHK05 Randomized Clinical Trial. JAMA. 2025 Mar 30:e253833. doi: 10.1001/jama.2025.3833. Epub ahead of print.
6. Anker SD, Kirwan BA, van Veldhuisen DJ, et al. Effects of ferric carboxymaltose on hospitalisations and mortality rates in iron-deficient heart failure patients: an individual patient data meta-analysis. Eur J Heart Fail. 2018 Jan;20(1):125-133. doi: 10.1002/ejhf.823. Epub 2017 Apr 24.
7. Auerbach M, Macdougall I. The available intravenous iron formulations: History, efficacy, and toxicology. Hemodial Int. 2017 Jun;21 Suppl 1:S83-S92. doi: 10.1111/hdi.12560. Epub 2017 Mar 29. PMID: 28371203.
8. Baker RD et al: Diagnosis and prevention of iron deficiency and iron-deficiency anemia in infants and young children (0-3 years of age). Pediatrics. 126(5):1040-50, 2010
9. Beck-da-Silva L, Piardi D, Soder S, et al. IRON-HF study: a randomized trial to assess the effects of iron in heart failure patients with anemia. Int J Cardiol. 2013 Oct 9;168(4):3439-42. doi: 10.1016/j.ijcard.2013.04.181. Epub 2013 May 13.
10. Bohlius J et al: Management of cancer-associated anemia with erythropoiesis-stimulating agents: ASCO/ASH clinical practice guideline update. Blood Adv. 3(8):1197-210, 2019
11. Camaschella C: Iron-deficiency anemia. N Engl J Med. 373(5):485-6, 2015
12. Chapter 1: diagnosis and evaluation of anemia in CKD. Kidney Int Suppl (2011). 2(4):288-91, 2012
13. Cho YW, Allen RP, Earley CJ. Lower molecular weight intravenous iron dextran for restless legs syndrome. Sleep Med. 2013;14(3):274-277. doi:10.1016/j.sleep.2012.11.001
14. Darwish AM, Khalifa EE, Rashad E, Farghally E. Total dose iron dextran infusion versus oral iron for treating iron deficiency anemia in pregnant women: a randomized controlled trial. J Matern Fetal Neonatal Med. 2019;32(3):398-403. doi:10.1080/14767058.2017.1379988
15. DeLoughery TG, Jackson CS, Ko CW, Rockey DC. AGA Clinical Practice Update on Management of Iron Deficiency Anemia: Expert Review. Clin Gastroenterol Hepatol. 2024 Aug;22(8):1575-1583. doi: 10.1016/j.cgh.2024.03.046. Epub 2024 Jun 12.
16. van Doren L, Steinheiser M, Boykin K, et al. Expert consensus guidelines: Intravenous iron uses, formulations, administration, and management of reactions. Am J Hematol. 2024 Jul;99(7):1338-1348. doi: 10.1002/ajh.27220. Epub 2024 Jan 29.
17. Earley CJ, Heckler D, Allen RP. Repeated IV doses of iron provides effective supplemental treatment of restless legs syndrome. Sleep Med. 2005 Jul;6(4):301-5. doi: 10.1016/j.sleep.2005.01.008. Epub 2005 Apr 1.
18. Feraheme (ferumoxytol) [prescribing information]. Waltham, MA: AMAG Pharmaceuticals, Inc; June 2022.
19. Ferrlecit (sodium ferric gluconate complex in sucrose) [prescribing information]. Bridgewater, NJ: Sanofi-Aventis US LLC; March 2022.
20. FIGO Working Group on Good Clinical Practice in Maternal-Fetal Medicine. Good clinical practice advice: iron deficiency anemia in pregnancy. Int J Gynaecol Obstet. 2019;144(3):322-324. doi:10.1002/ijgo.12740
21. Gutiérrez O. Treatment of iron deficiency anemia in CKD and end-stage kidney disease. Kidney Int Rep. 2021;6(9):2261-2269. doi:10.1016/j.ekir.2021.05.020
22. Heidenreich PA, Bozkurt B, Aguilar D, Allen LA, Byun JJ, Colvin MM, Deswal A, Drazner MH, Dunlay SM, Evers LR, Fang JC, Fedson SE, Fonarow GC, Hayek SS, Hernandez AF, Khazanie P, Kittleson MM, Lee CS, Link MS, Milano CA, Nnacheta LC, Sandhu AT, Stevenson LW, Vardeny O, Vest AR, Yancy CW. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. J Am Coll Cardiol. 2022 May 3;79(17):e263-e421. doi:

10.1016/j.jacc.2021.12.012. Epub 2022 Apr 1. Erratum in: J Am Coll Cardiol. 2023 Apr 18;81(15):1551. PMID: 35379503.
23. INFeD (iron dextran complex) [prescribing information]. Madison, NJ: Allergan USA Inc; August 2024.
24. Injectafer (ferric carboxymaltose) [prescribing information]. Shirley, NY: American Regent Inc; January 2025.
25. Iolascon A, Andolfo I, Russo R, et al. Recommendations for diagnosis, treatment, and prevention of iron deficiency and iron deficiency anemia. Hemasphere. 2024 Jul 15;8(7):e108. doi: 10.1002/hem3.108.
26. Kalra PR, Cleland JGF, Petrie MC, et al. Intravenous ferric derisomaltose in patients with heart failure and iron deficiency in the UK (IRONMAN): an investigator-initiated, prospective, randomised, open-label, blinded-endpoint trial. Lancet. 2022 Dec 17;400(10369):2199-2209. doi: 10.1016/S0140-6736(22)02083-9. Epub 2022 Nov 5.
27. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 clinical practice guidelines for anemia in chronic kidney disease (2012). https://kdigo.org/wp-content/uploads/2016/10/KDIGO-2012-Anemia-Guideline-English.pdf.
28. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 clinical practice guidelines for the evaluation and management of chronic kidney disease. Kidney Inter. 2013;3(suppl):1-150. http://kdigo.org/clinical_practice_guidelines/pdf/KDIGO-Anemia%20GL.pdf
29. Ko CW et al: AGA clinical practice guidelines on the gastrointestinal evaluation of iron deficiency anemia. Gastroenterology. 159(3):1085-94, 2020
30. Lopez A et al: Iron deficiency anaemia. Lancet. 387(10021):907-16, 2016
31. Macdougall IC et al: Intravenous iron in patients undergoing maintenance hemodialysis. N Engl J Med. 380(5):447-58, 2019
32. McDonagh T et al: Screening, diagnosis and treatment of iron deficiency in chronic heart failure: putting the 2016 European Society of Cardiology heart failure guidelines into clinical practice. Eur J Heart Fail. 20(12):1664-72, 2018
33. Means RT: Approach to the anemias. In: Goldman L et al, eds: Goldman-Cecil Medicine. 26th ed. Elsevier, 2020:1028-35.e1
34. Mentz RJ, Garg J, Rockhold FW, et al. Ferric Carboxymaltose in Heart Failure with Iron Deficiency. N Engl J Med. 2023 Sep 14;389(11):975-986. doi: 10.1056/NEJMoa2304968. Epub 2023 Aug 26.
35. Monoferric (ferric derisomaltose) [prescribing information]. Morristown, NJ: Pharmacosmos Therapeutics Inc; August 2022.
36. NIH: Iron Fact Sheet for Professionals. NIH website. Updated June 15, 2023. Accessed April 10, 2024. https://ods.od.nih.gov/factsheets/Iron-HealthProfessional/#h2
37. Pavord S, Daru J, Prasannan N, Robinson S, Stanworth S, Girling J; BSH Committee. UK guidelines on the management of iron deficiency in pregnancy. Br J Haematol. 2020 Mar;188(6):819-830. doi: 10.1111/bjh.16221. Epub 2019 Oct 2. PMID: 31578718.
38. Percy L, Mansour D, Fraser I. Iron deficiency and iron deficiency anaemia in women. Best Pract Res Clin Obstet Gynaecol. 2017 Apr;40:55-67. doi: 10.1016/j.bpobgyn.2016.09.007. Epub 2016 Oct 1. PMID: 28029503.
39. Ponikowski P, Kirwan BA, Anker SD, et al. Ferric carboxymaltose for iron deficiency at discharge after acute heart failure: a multicentre, double-blind, randomised, controlled trial. Lancet. 2020 Dec 12;396(10266):1895-1904. doi: 10.1016/S0140-6736(20)32339-4. Epub 2020 Nov 13. Erratum in: Lancet. 2021 Nov 27;398(10315):1964. doi: 10.1016/S0140-6736(21)02492-2.
40. Ponikowski P, Mentz RJ, Hernandez AF, et al. Efficacy of ferric carboxymaltose in heart failure with iron deficiency: an individual patient data meta-analysis. Eur Heart J. 2023 Dec 21;44(48):5077-5091. doi: 10.1093/eurheartj/ehad586.
41. Ponikowski P, van Veldhuisen DJ, Comin-Colet J, et al. Beneficial effects of long-term intravenous iron therapy with ferric carboxymaltose in patients with symptomatic heart failure and iron deficiency†. Eur Heart J. 2015 Mar 14;36(11):657-68. doi: 10.1093/eurheartj/ehu385. Epub 2014 Aug 31.

42. Powers JM et al: Diagnosis and management of iron deficiency anemia. Hematol Oncol Clin North Am. 28(4):729-45, vi-vii, 2014
43. Rocha BML et al: The burden of iron deficiency in heart failure: therapeutic approach. J Am Coll Cardiol. 71(7):782-93, 2018
44. Short MW et al: Iron deficiency anemia: evaluation and management. Am Fam Physician. 87(2):98-104, 2013
45. Silber MH, Buchfuhrer MJ, Earley CJ, et al. The Management of Restless Legs Syndrome: An Updated Algorithm. Mayo Clin Proc. 2021 Jul;96(7):1921-1937. doi: 10.1016/j.mayocp.2020.12.026.
46. Siu AL; US Preventive Services Task Force. Screening for iron deficiency anemia and iron supplementation in pregnant women to improve maternal health and birth outcomes: US Preventive Services Task Force Recommendation Statement. Ann Intern Med. 2015;163(7):529-536. doi:10.7326/M15-1707
47. Trotti LM et al: Iron for the treatment of restless legs syndrome. Cochrane Database Syst Rev. 1:CD007834, 2019
48. Venofer (iron sucrose) [prescribing information]. Shirley, NY: American Regent Inc; July 2022.
49. Wong L et al: Safety and efficacy of rapid (1,000 mg in 1 hr) intravenous iron dextran for treatment of maternal iron deficient anemia of pregnancy. Am J Hematol. 91(6):590-3, 2016
50. World Health Organization (WHO). Guideline: Iron Supplementation in Postpartum Women. World Health Organization; 2016.
51. World Health Organization (WHO). Guideline on haemoglobin cutoffs to define anaemia in individuals and populations. [Internet]. Geneva: World Health Organizations; 2024. Accessed 20 May 2025.
52. World Health Organization (WHO). Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. Vitamin and Mineral Nutrition Information System. https://iris.who.int/bitstream/handle/10665/85839/WHO_NMH_NHD_MNM_11.1_eng.pdf?sequence=22. Published 2011.
53. World Health Organization (WHO). Serum ferritin concentrations for the assessment of iron status in individuals and populations: technical brief. https://iris.who.int/bitstream/handle/10665/337666/9789240008526-eng.pdf?sequence=1. Published 2020.
54. Yancy CW et al: 2017 ACC/AHA/HFSA focused update of the 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Task Force on clinical practice guidelines and the Heart Failure Society of America. J Card Fail. 23(8):628-51, 2017

Clinical Guideline Revision / History Information

Original Date: 4/26/2024

Reviewed/Revised: 8/29/2024, 12/02/2024, 11/01/2025