# Injectable Iron Products

Policy Number: MC/PC 022
Effective Date: May 1, 2025

Instructions for Use

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**Related Policies**

- N/A

## Coverage Rationale

### This policy refers to the following injectable iron products:

- Feraheme® (ferumoxytol injection)
- Injectafer® (ferric carboxymaltose injection)
- Monoferric (ferric derisomaltose injection)

### For initial coverage of Feraheme or Monoferric, the following will be required:

- Requested drug is being used for a Food and Drug Administration (FDA)-approved indication **and**
- Patient has diagnosis of chronic kidney disease (CKD) **and**
- Trial and failure of a minimum 30-day supply or intolerance to one oral iron therapy (e.g., ferrous sulfate, ferrous gluconate, ferrous fumarate) or attestation demonstrating a trial with oral iron therapies may be inappropriate.

### For initial coverage of Injectafer, the following will be required:

- Requested drug is being used for a Food and Drug Administration (FDA)-approved indication **and**
- One of the following:
  - Trial and failure of a minimum 30-day supply or intolerance to one oral iron therapy (e.g., ferrous sulfate, ferrous gluconate, ferrous fumarate) or attestation demonstrating a trial with oral iron therapies may be inappropriate **or**
  - Patient has New York Heart Association class II or III Heart Failure

## Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan

| HCPCS Code | Description |
|---|---|
| J1437 | Injection, ferric derisomaltose, 10 mg |
| J1439 | Injection, ferric carboxymaltose, 1 mg |
| Q0138 | Injection, ferumoxytol, for treatment of iron deficiency anemia, 1 mg (non-ESRD use) |

| ICD-10 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 |
| D63.1 | Anemia in chronic kidney disease |
| I12.9 | Hypertensive chronic kidney disease with stage 1 through stage 4 chronic kidney disease, or unspecified chronic kidney disease |
| I13.0 | Hypertensive heart and chronic kidney disease with heart failure and stage 1 through stage 4 chronic<br>kidney disease, or unspecified chronic kidney disease |
| I13.10 | Hypertensive heart and chronic kidney disease without heart failure, with stage 1 through stage 4 chronic kidney disease, or unspecified chronic kidney disease |
| I50.1 | Left ventricular failure, unspecified |
| 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 |
| I50.30 | 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 |
| I50.40 | 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 |
| I50.810 | 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 |

| ICD-10 Code | Description |
|---|---|
| I50.89 | Other heart failure |
| I50.9 | Heart failure, unspecified |
| N18.1 | Chronic kidney disease, stage 1 |
| N18.2 | Chronic kidney disease, stage 2 (mild) |
| 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 |

## Background

More than a quarter of the world's population is anemic; more than 12% of these cases are due to iron deficiency (ID). A large proportion of cases are in women of childbearing age, children, and individuals living in low- and middle-income countries (*Auerbach & DeLoughery 2023*). Anemia has been shown to worsen heart failure (HF) and is associated with increased mortality in patients with chronic HF. Anemia is also associated with worse outcomes after cardiac and non-cardiac surgery, including increased mortality and length of hospital stay (*Clevenger et al 2016*). The World Health Organization (WHO) defines anemia as a circulating hemoglobin (Hb) level of < 12 g/dL in non-pregnant women over age 15 years, < 13 g/dL in men over age 15 years, and < 11 g/dL in pregnant women (*WHO Web site*). Iron Deficiency is more prevalent than Iron Deficiency Anemia (IDA) (low Hb or hematocrit [Hct] caused by ID) and females are affected more than males. The greater prevalence of ID and IDA in females of childbearing age is attributed to menstruation and childbirth (*Auerbach 2025*). Some individuals with absent or reduced iron stores who have not yet developed anemia may have symptoms such as fatigue or reduced exercise tolerance (*Auerbach & DeLoughery 2025*).

For treatment of ID, the choice between oral and IV iron depends on several factors including the acuity of the anemia, costs and availability of different iron replacement products, and patient tolerability. Most patients are treated with oral iron because it is generally effective, readily available, inexpensive, and safe. IV administration of iron may be preferable to the oral route in patients with ongoing blood loss, a physiologic or anatomic abnormality that interferes with oral absorption or iron homeostasis, and intolerable gastrointestinal adverse effects (AEs) of oral iron (especially ferrous sulfate). In general, the various oral iron preparations are equally effective (*Auerbach & DeLoughery 2025*).

Anemia is common among patients with chronic kidney disease (CKD), including those on dialysis; ID is the most common reversible cause (*Berns 2025*). Hemodialysis (HD) patients may experience repeated blood loss due to retention of blood in the dialyzer and blood lines. Other contributing causes in HD and other CKD patients include frequent blood sampling for laboratory testing, blood loss from surgical procedures (such as creation of vascular access), interference with iron absorption due to medications such as gastric acid inhibitors and phosphate binders, and reduced iron absorption due to inflammation (*Kidney Disease Improving Global Outcomes [KDIGO] 2012*). For HD or peritoneal dialysis (PD) patients requiring iron therapy, IV rather than oral iron therapy is recommended. For PD patients, oral iron may be used in patients with limited IV access and who require preservation of sites for HD access, particularly if anemia and ID are mild. For maintenance HD patients, IV iron is more effective than oral iron in increasing Hb concentration and iron stores (*Berns 2023*).
For non-dialysis-dependent (NDD)-CKD patients, oral iron is usually used. NDD-CKD patients who are candidates for IV iron include those who require more rapid repletion of iron, who cannot tolerate oral iron, or who are unlikely to be effectively treated with oral iron, including most patients with symptomatic anemia, provided that red blood cell (RBC) transfusion can be safely deferred (*Berns 20243*).

**Comparisons of IV iron with oral iron**

*Clevenger et al 2016* conducted a systematic review and meta-analysis of 65 randomized controlled trials (RCTs) (N = 9004) in adults with IDA without CKD. The primary outcome was mortality at 1 year. Only 1 study (comparing parenteral with oral iron) reported mortality at 1 year. Eight studies of oral iron vs inactive control, 19 studies of parenteral iron vs inactive control, and 13 studies of parenteral iron vs oral iron reported mortality. There were no statistically significant differences in mortality in any of the comparisons. Both oral and parenteral iron significantly reduced the proportion of patients requiring RBC blood transfusion compared with control (risk ratio [RR] 0.66, 95% confidence interval [CI], 0.48 to 0.90; and RR 0.84, 95% CI, 0.73 to 0.97, respectively). Hb was increased more by both oral and parenteral iron compared with control (mean difference [MD] 0.91 g/dL, 95% CI, 0.48 to 1.35; and MD 1.04, 95% CI, 0.52 to 1.57, respectively), and parenteral iron demonstrated a greater increase when compared with oral iron (MD 0.53 g/dL; 95% CI, 0.31 to 0.75). In all comparisons, there were no differences in the results comparing patients with and without heart failure (HF). Six trials reported quality of life (QoL) with parenteral iron vs control and found higher QoL in the parenteral iron group. There was no significant difference in QoL with parenteral vs oral iron. There were no statistically significant differences in serious adverse effects (SAEs) between parenteral iron and control. No trials reported severe allergic reactions from parenteral iron. There was no statistically significant difference in SAEs with parenteral vs oral iron.

A Cochrane review of 39 RCTs (N = 3852) was conducted to compare IV iron with oral iron for anemia in adults and children with CKD stages 3 to 5 receiving HD or PD, not receiving dialysis, or post kidney transplant (*O'Lone et al 2019*). The primary outcomes were all-cause mortality, cardiovascular (CV) death, and QoL. There was insufficient evidence to determine whether all-cause death differed between IV iron and oral iron (absolute risk 33 vs 30 per 1000; RR 1.12; 95% CI, 0.64 to 1.94; I2 = 0%, low certainty evidence). It was also uncertain whether CV death differed between IV and oral iron, (RR 1.71; 95% CI, 0.41 to 7.18; I2 = 0%, very low certainty evidence). Compared with oral iron, IV iron increased the number of patients achieving target Hb (absolute benefit 542 vs 317 per 1000; RR 1.71; 95% CI, 1.43 to 2.04), increased Hb (MD 0.72 g/dL, 95% CI, 0.39 to 1.05); ferritin (MD 224.84 mcg/L; 95% CI, 165.85 to 283.83) and transferrin saturation (TSAT) (MD 7.69%; 95% CI, 5.10 to 10.28), and reduced the ESA dose required (standardized mean difference [SMD] -0.72; 95% CI, -1.12 to -0.31). All analyses had low certainty evidence and moderate to high heterogeneity. Compared with oral iron, IV iron increased the numbers of patients who experienced allergic reactions or hypotension (RR 3.56; 95% CI, 1.88 to 6.74) but reduced the number with all GI AEs (RR 0.47; 95% CI, 0.33 to 0.66). The certainty of evidence was low. There was insufficient evidence to determine impact on QoL.

A systematic review and meta-analysis of 75 RCTs (N = 10,605) evaluated the efficacy (change in Hb concentration and proportion of patients requiring allogeneic RBC transfusion) and safety (all-cause infection) of IV iron compared with oral iron or no iron (*Litton et al 2013*). IV iron was associated with a significant increase in standardized mean Hb (6.5 g/L; 95% CI, 5.1 g/L to 7.9 g/L; I2 = 87.7%, $p < 0.01$) and a significant reduction in risk of blood transfusion (RR 0.74; 95% CI, 0.62 to 0.88; I2 = 9%, $p = 0.3$). There was no significant difference in mortality (RR 1.1; 95% CI, 0.8 to 1.5) or SAEs (RR 1.1; 95% CI, 0.9 to 1.2) with IV iron therapy compared with oral iron or no iron. IV iron was associated with a significant increase in the risk of infection compared with either oral iron or no iron (RR 1.33; 95% CI, 1.10 to 1.64; I2 = 22.7%, $p = 0.2$).

A systematic review and meta-analysis of 11 RCTs (IV iron: N = 599; oral iron; N = 591) comparing IV with oral iron for the treatment of IDA in pregnancy found that IV iron was superior to oral iron (*Govindappagari & Burwick 2019*). For the co-primary endpoints, pregnant women receiving IV iron achieved target Hb more often (pooled odds ratio [OR] 2.66; 95% CI, 1.71 to 4.15; $p < 0.001$; I2 = 47%); had a greater increase in Hb after 4 weeks (pooled weighted mean difference [WMD] 0.84 g/dL; 95% CI, 0.59 to 1.09; $p < 0.001$; and had fewer AEs (pooled OR 0.35; 95% CI, 0.18 to 0.67; $p = 0.001$; I2 = 74%) vs oral iron.

A systematic review and meta-analysis of 5 RCTs (N = 694) compared IV iron with oral iron for the treatment of IDA in patients with inflammatory bowel disease (IBD) (*Bonovas et al 2016*). The primary outcome was the effect of treatment

on the Hb response (increase of ≥ 2.0 g/dL at the end of the follow-up). A greater [illegible] ents achieved a significantly greater increase in Hb ≥ 2.0 g/dL than oral iron-treated [illegible] 18). Treatment discontinuation rates due to AEs or intolerance were lower with IV iron (OR 0.27; 95% CI, 0.13 to 0.59). Similarly, the occurrence of GI AEs was lower in the IV iron groups. SAEs were more frequently reported among patients receiving IV iron (OR 4.57; 95% CI, 1.11 to 18.8); however, the majority were judged as unrelated or unlikely to be related to the study medication.

**Comparative trials of IV iron products**

Multiple trials and meta-analyses comparing various IV iron products have generally found similar efficacy and safety among agents. A systematic review and network meta-analysis of 21 RCTs comparing the efficacy and safety of ferric carboxymaltose (Injectafer) with other iron formulations in patients with iron deficiency (ID) found that all IV iron preparations appeared to be safe and effective, but ferric carboxymaltose seemed to provide a better and quicker correction of Hb and serum ferritin levels in patients with ID (*Rognoni et al 2016*). The mean difference (MD) in Hb over the study period was significantly larger for ferric carboxymaltose compared to ferric gluconate (Ferrlecit) (delta 0.6; 95% CI, 0.2 to 0.9). Ferric carboxymaltose was superior to iron sucrose (Venofer) with a delta of 1.1 (95% CI, to 1.8 to 3.9) but without statistical significance. All IV iron products were well tolerated, with no anaphylactic reactions reported.

A systematic review and meta-analysis of 9 RCTs (N = 5691) was conducted to compare the safety and efficacy of ferumoxytol (Feraheme) in the treatment of ID (with or without anemia) to other IV iron formulations, oral iron, or placebo (*Abdulrehman et al 2019*). The results indicated little to no difference in treatment emergent adverse events (TEAEs) (RR 0.88; 95% CI, 0.80 to 0.97), treatment-related adverse events (TRAEs) (RR 0.73; 95% CI, 0.61 to 0.88), serious adverse events (SAEs) (RR 1.13; 95% CI, 0.77 to 1.67), related serious adverse events (RSAEs) (RR 0.55; 95% CI, 0.05 to 6.16), hypotension or hypersensitivity reactions (HSRs) (RR 0.58; 95% CI, 0.31 to 1.09), or composite cardiovascular (CV) outcomes (RR 0.56; 95% CI, 0.24 to 1.29) when comparing ferumoxytol to other IV iron products; there was also little to no difference in the number of patients achieving an increase in Hb of ≥ 1 g/dL (RR 1.04; 95% CI, 0.96 to 1.12). Ferumoxytol was associated with fewer TEAEs compared to oral iron (RR 0.78; 95% CI, 0.61 to 0.98), but more compared to placebo (RR 1.62; 95% CI, 1.01 to 2.61).

A systematic literature review of RCTs indirectly compared the efficacy of iron isomaltoside (Monoferric) and ferric carboxymaltose (Injectafer) in patients with IDA (*Pollock & Muduma 2019*). The indirect treatment comparison (ITC) using comparative trials of iron sucrose (Venofer) vs iron isomaltoside and iron sucrose vs ferric carboxymaltose resulted in a significantly larger increase from baseline in Hb with iron isomaltoside relative to ferric carboxymaltose (MD of +0.249 g/dL), but there was no significant difference in the proportion of patients with a clinically relevant response.

A 5-week, Phase 3, double-blind (DB), multicenter (MC), RCT compared the safety and efficacy of ferumoxytol (Feraheme) with ferric carboxymaltose (Injectafer) in 1997 adults with IDA (*Adkinson et al 2018*). For the primary endpoint of the composite incidences of moderate-to-severe HSRs, including anaphylaxis, or moderate-to-severe hypotension, ferumoxytol and ferric carboxymaltose were shown to be noninferior (0.6% and 0.7%, respectively). No anaphylaxis was reported in either group. Least-squares (LS) mean changes in Hb were 1.4 and 1.6 g/dL in the ferumoxytol and ferric carboxymaltose groups, meeting the criteria for noninferiority. Hypophosphatemia occurred in 0.4% in the ferumoxytol group and 38.7% in the ferric carboxymaltose group; however, no clinical sequelae related to hypophosphatemia were seen in either group.

*Hetzel et al 2014* conducted an open-label (OL), active-controlled (AC), MC trial to compare the efficacy and safety of ferumoxytol (Feraheme) with iron sucrose (Venofer) for the treatment of IDA (N = 605). An Hb increase of ≥ 2 g/dL was achieved in 84 vs 81.4% of patients treated with ferumoxytol and iron sucrose, respectively, demonstrating noninferiority. Drug-related AEs were reported in 14.3% of the Feraheme group vs 16.1% of the iron sucrose group. SAEs were observed at a slightly higher rate in the ferumoxytol treatment group compared with the iron sucrose treatment group (4.2 vs 2.5%). Iron sucrose-treated patients had a higher incidence of moderate-to-severe hypotension occurring on the day of dosing and moderate-to-severe HSRs occurring within 48 hours post dose compared with ferumoxytol-treated patients (5.0 vs 2.7%).

A 7-week, Phase 2, OL, AC, MC, randomized trial compared the safety and effic ron sucrose (Venofer) in 162 patients with hemodialysis-dependent (HDD) or NDD-CKD and IDA (*Macdougall et al 2014*). The change in Hb from baseline to week 5 adjusted for baseline Hb and dialysis status was 0.8 ± 0.1 g/dL for Feraheme and 0.7 ± 0.1 g/dL for Venofer (difference = 0.1 g/dL); criteria for noninferiority were met. The AE profile of the 2 treatment groups was similar. SAEs were reported in 9% of ferumoxytol vs 7% of iron sucrose patients; the rate of related SAEs was 1% in both groups. Overall, adverse events of special interest (AESIs, defined as moderate or severe hypotension requiring medical intervention or hospitalization, acute decreases in systolic blood pressure from baseline of ≥ 30% during the 60-minute post-dose observation period, hypotension associated with symptoms, systemic allergic reactions [anaphylaxis/anaphylactoid reactions], and milder symptoms of hypersensitivity) occurred in 1.3% of ferumoxytol-treated patients and 6.1% of iron sucrose-treated patients.

A randomized, OL, MC trial (FERWON-IDA) compared ferric derisomaltose (Monoferric) with iron sucrose (Venofer) in 1512 adults with IDA with intolerance or lack of response to oral iron or screening Hb measurement sufficiently low to require rapid repletion of iron stores (*Auerbach et al 2019*). The frequency of patients with serious or severe HSRs was 0.3 vs 0.4% in the Monoferric and Venofer group, respectively. Eight composite cardiovascular (CV) AEs were reported in 8 (0.8%) patients in the ferric derisomaltose group, and 7 were reported in 6 (1.2%) patients in the iron sucrose group ($p > 0.05$). The change in Hb concentration from baseline to week 8 was noninferior for ferric derisomaltose compared to iron sucrose (LS mean change in Hb = 2.49 g/dL in both groups). The incidence of severe hypophosphatemia (phosphate < 1.0 mg/dL) was 0.0% in both groups. Improvements in Functional Assessment of Chronic Illness Therapy (FACIT) fatigues scores were similar in both groups.

A randomized, OL, MC trial (FERWON-NEPHRO) compared the safety and efficacy of ferric derisomaltose (Monoferric) (n = 1027) and iron sucrose (Venofer) (n = 511) in patients with CKD (*Bhandari et al 2020*). There was no significant difference in the incidence of serious or severe HSRs in the ferric derisomaltose and iron sucrose groups (0.3% vs 0%; risk difference: 0.29%; 95% CI, -0.19 to 0.77; $p > 0.05$). The incidence of composite CV AEs was significantly lower in the ferric derisomaltose vs iron sucrose group (55 events in 42 patients [4.1%] vs 41 events in 35 patients [6.9%]; $p = 0.025$). The change in Hb from baseline to week 8 showed non-inferiority (1.22 vs 1.14 g/dL [difference for ferric derisomaltose – iron sucrose = 0.08; 95% CI, -0.06 to 0.23]; $p = 0.27$). The incidence of hypophosphatemia (serum phosphate < 2.0 mg/dL) was 3.2% in the ferric derisomaltose and 0.8% in the iron sucrose group ($p = 0.004$); no patient in either group developed severe hypophosphatemia (serum phosphate < 1.0 mg/dL). Improvements in FACIT fatigue scores were similar in both groups.

A pre-specified combined safety analysis of FERWON-IDA and FERWON-NEPHRO (N = 3050) (*Wolf et al 2021*) found no significant differences in the incidence of mild, moderate, or severe HSRs between the ferric derisomaltose (Monoferric) and iron sucrose (Venofer) groups; adjudicated serious or severe HSRs occurred in 0.3% vs 0.2%, respectively, meeting criteria for non-inferiority. The incidence of composite CV AEs was significantly lower in the ferric derisomaltose group compared with the iron sucrose group (2.5% vs 4.1%; $p = 0.018$). In post-hoc analyses, there were no significant differences between ferric derisomaltose and iron sucrose in the incidence of mild, moderate, or severe AEs.

Two identically designed, 35-day, OL, MC, randomized trials (PHOSPHARE) compared the risk of hypophosphatemia and effects on biomarkers of mineral and bone homeostasis of IV ferric derisomaltose (Monoferric) vs ferric carboxymaltose (Injectafer) in 245 adults with IDA and a history of intolerance or unresponsiveness to oral iron (*Wolf et al 2020*). The incidence of hypophosphatemia at any time between baseline and day 35 was significantly lower among patients treated with ferric derisomaltose than with ferric carboxymaltose (trial A: 7.9% vs 75.0% [adjusted rate difference, -67.0% {95% CI, -77.4% to -51.5%}], $p < 0.001$; trial B: 8.1% vs 73.7% [adjusted rate difference, -65.8% {95% CI, -76.6% to -49.8%}], $p < 0.001$. The clinical relevance of this difference has not been established and clinical outcomes were not assessed. In the pooled analysis, the change in Hb level per g of iron infused on day 35 was 2.2 vs 2.0 g/dL for ferric derisomaltose vs ferric carboxymaltose ($p = 0.02$). Hb level (exploratory endpoint) was 11.9 vs 12.4 g/dL, respectively; $p < 0.001$.

**Heart failure (HF)**
A systematic review and meta-analysis evaluated the efficacy and safety of IV i [illegible] heart failure (HF) and ID (5 RCTs, N = 907) (*Qian et al 2016*). The primary outcomes were hospitalization for HF, all-cause mortality, and a combined endpoint of hospitalization for HF and death. Ferric carboxymaltose (Injectafer) and iron sucrose (Venofer) were used in 2 trials each vs control and 1 trial used both vs control. There was a significantly reduced rate of hospitalization for HF among patients receiving iron compared with the non-iron treatment group (OR 0.28; 95% CI, 0.16 to 0.49; p < 0.001). There was no significant difference in all-cause mortality between the iron and non-iron groups (OR 0.81; 95% CI, 0.42 to 1.57; p = 0.53). The iron group had a significant decrease in the risk of the composite of hospitalization for HF and death (OR 0.47; 95% CI, 0.29 to 0.76; p = 0.002). The iron group had a statistically lower rate of SAEs than the control group (OR 0.50; 95% CI, 0.34 to 0.75; p = 0.001). Of the AEs reported in the included studies, such as CV, nervous system, GI, and vascular disorders, none was observed to occur more frequently in the iron group. In addition, no severe allergic reactions related to IV iron were reported in any of included trials.

**Place in Therapy**
Several clinical guidelines have been published addressing ID and IDA in various patient populations. None of these guidelines express a preference for any specific iron preparation over another.

The Kidney Disease Improving Global Outcomes (KDIGO) guidelines for anemia of CKD (*KDIGO 2012*) make the following recommendations with regard to iron supplementation:

- The potential benefits of avoiding or minimizing blood transfusions, erythropoiesis-stimulating agent (ESA) therapy, and anemia-related symptoms should be balanced against the risks of harm in individual patients (e.g., anaphylactoid and other acute reactions, unknown long-term risks).
- In adults with CKD not on iron or ESA therapy, a trial of IV iron (or alternatively a 1- to 3-month trial of oral iron in NDD-CKD patients) is suggested if:
    - an increase in Hb concentration without starting ESA treatment is desired and
    - transferrin saturation (TSAT) is ≤ 30% and ferritin is ≤ 500 ng/mL
- In adult CKD patients on ESA therapy who are not receiving iron supplementation, a trial of IV iron (or alternatively in NDD-CKD patients, a 1- to 3-month trial of oral iron therapy) is suggested if:
    - an increase in Hb concentration or a decrease in ESA dose is desired and
    - TSAT is ≤ 30% and ferritin is ≤ 500 ng/mL
- For NDD-CKD patients who require iron supplementation, the route of iron administration should be based on the severity of ID, availability of venous access, response to prior oral iron therapy, AEs with prior oral or IV iron therapy, patient compliance, and cost.
- When the initial dose of IV iron dextran is administered, it is recommended, and when the initial dose of IV non-dextran iron is administered, it is suggested, that patients be monitored for 60 minutes after the infusion and that resuscitative facilities and personnel trained to evaluate and treat SAEs be available.
- Administration of IV iron to patients with active systemic infection should be avoided.

The U.S. Preventative Services Task Force (USPSTF) Screening for IDA and Iron Supplementation in Pregnant Women to Improve Maternal Health and Birth Outcomes recommendation statement (*Siu 2015*) concluded that the current evidence is insufficient to assess the balance of benefits and harms of screening for IDA in pregnant women to prevent adverse maternal health and birth outcomes and that the evidence on the effect of routine iron supplementation during pregnancy on maternal health or birth outcomes, such as maternal IDA, cesarean delivery, preterm delivery, infant mortality, or low birthweight was inadequate.
IDA in pregnant women is treated through additional iron intake with oral iron pills (usually 60 to 120 mg of elemental iron per day) and diet. IV iron treatment can also be used during pregnancy.

The American College of Cardiology/American Heart Association/Heart Failure Society of America (ACC/AHA/HFSA) Guideline for the Management of HF (*Yancy et al 2022*) provides a recommendation regarding IDA in patients with HF. Anemia is independently associated with HF disease severity, and ID appears to be uniquely associated with reduced

exercise capacity. IV repletion of iron, especially in the setting of concomitant I ve exercise capacity and QoL. There is an uncertain evidence base for oral iron re iated with HF. In patients with New York Heart Association (NYHA) class II and III HF and ID (ferritin < 100 ng/mL or 100 to 300 ng/mL if TSAT is < 20%), IV iron has been shown to improve exercise capacity and QoL (Class of recommendation [COR] IIa [moderate ], level of evidence [LOE] B-R [moderate-quality evidence from 1 or more RCTs or meta-analyses of moderate-quality RCTs]).

## U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

**Feraheme** is an iron replacement product indicated for the treatment of iron deficiency anemia (IDA) in adult patients:

- who have intolerance to oral iron or have had unsatisfactory response to oral iron or
- who have chronic kidney disease (CKD).

**Injectafer** is an iron replacement product indicated for the treatment of:

- iron deficiency anemia (IDA) in:
  - adult and pediatric patients 1 year of age and older who have either intolerance or an unsatisfactory response to oral iron.
  - adult patients who have non-dialysis dependent chronic kidney disease.
- iron deficiency in adult patients with heart failure and New York Heart Association class II/III to improve exercise capacity.

**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.
- who have non-hemodialysis dependent chronic kidney disease.

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## Policy History/Revision Information

| Date | Summary of Changes |
|---|---|
| 12/13/2023 | Approved by OptumRx P&T Committee |
| 4/17/2024 | Annual Review. Updated references. |
| 4/16/2025 | Annual Review. Updated references. |

## Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. The insurance reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

OptumRx may also use tools developed by third parties to assist us in administering health benefits. OptumRx Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

## Archived Policy Versions (Internal Only)

| Effective Date | Policy Number | Policy Title |
|---|---|---|
| mm/dd/yyyy – mm/dd/yyyy | ###### | Title of Policy Hyperlinked to KL or Other Internal Location |

# Nondiscrimination & Language Access Policy

Discrimination is Against the Law. Aspirus Health Plan, Inc. complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex, (including sex characteristics, including intersex traits; pregnancy or related conditions; sexual orientation, gender identity and sex stereotypes), consistent with the scope of sex discrimination described at 45 CFR § 92.101(a)(2). Aspirus Health Plan, Inc. does not exclude people or treat them less favorably because of race, color, national origin, age, disability, or sex.

Aspirus Health Plan, Inc.:
Provides people with disabilities reasonable modifications and free appropriate auxiliary aids and services to communicate effectively with us, such as:

- Qualified sign language interpreters.
- Written information in other formats (large print, audio, accessible electronic formats, other formats).

Provides free language assistance services to people whose primary language is not English, which may include:

- Qualified interpreters.
- Information written in other languages.

If *you* need reasonable modifications, appropriate auxiliary aids and services, or language assistance services, contact the Nondiscrimination Grievance Coordinator at the address, phone number, fax number, or email address below.

If *you* believe that Aspirus Health Plan, Inc. has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex, *you* can file a *grievance* with:

Nondiscrimination Grievance Coordinator
Aspirus Health Plan, Inc.
PO Box 1890
Southampton, PA 18966-9998
Phone: 1-866-631-5404 (TTY: 711)
Fax: 763-847-4010
Email: customerservice@aspirushealthplan.com

*You* can file a *grievance* in person or by mail, fax, or email. If *you* need help filing a *grievance*, the Nondiscrimination Grievance Coordinator is available to help *you*.

*You* can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:

U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
1.800.368.1019, 800.537.7697 (TDD)

Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html. This notice is available at Aspirus Health Plan, Inc.'s website: https://aspirushealthplan.com/webdocs/70021-AHP-NonDiscrim_Lang-Assist-Notice.pdf.

## Language Assistance Services

**Albanian**: KUJDES: Nëse flitni shqip, për ju ka në dispozicion shërbime të asistencës gjuhësore, pa pagesë.Telefononi në 1-800-332-6501 (TTY: 711).

**Arabic** تنبيه: إذا كنت تتحدث اللغة العربية، فإن خدمات المساعدة اللغوية متاحة لك مجاناً. اتصل بن اعلى رقم الهاتف1-800-332-6501(رقم هاتف الصم والبك : 711)

**French**: ATTENTION: Si vous parlez français, des services d'aide linguistique vous sont proposés gratuitement. Appelez le 1-800-332-6501 (ATS: 711).

**German**: ACHTUNG: Wenn Sie Deutsch sprechen, stehen Ihnen kostenlos sprachliche Hilfsdienstleistungen zurVerfügung. Rufnummer: 1-800-332-6501 (TTY: 711).

**Hindi**: _यान द_: य_द आप ि हंदी बोलते ह_ तो आपके ि लए मु_त म_ भाषा सहायता सेवाएं उपल_ध ह_।1-800-332-6501 (TTY: 711) पर कॉल कर_।

**Hmong**: LUS CEEV: Yog tias koj hais lus Hmoob, cov kev pab txog lus, muaj kev pab dawb rau koj. Hu rau 1-800-332-6501 (TTY: 711).

**Korean**: 주의: 한국어를 사용하시는 경우, 언어 지원 서비스를 무료로 이용하실 수 있습니다.1-800-332-6501 (TTY: 711)번으로 전화해 주십시오.

**Polish**: UWAGA: Jeżeli mówisz po polsku, możesz skorzystać z bezpłatnej pomocy językowej. Zadzwoń pod numer1-800-332-6501 (TTY: 711).

**Russian**: ВНИМАНИЕ: Если вы говорите на русском языке, то вам доступны бесплатные услуги перевода.Звоните 1-800-332-6501 (телетайп: 711).

**Spanish**: ATENCIÓN: si habla español, tiene a su disposición servicios gratuitos de asistencia lingüística. Llame al1-800-332-6501 (TTY: 711).

**Tagalog**: PAUNAWA: Kung nagsasalita ka ng Tagalog, maaari kang gumamit ng mga serbisyo ng tulong sa wika nangwalang bayad. Tumawag sa 1-800-332-6501 (TTY: 711).

**Traditional Chinese**: 注意：如果您使用繁體中文， 您可以免費獲得語言援助服務。請 致電 1-800-332-6501 (TTY: 711)

**Vietnamese**: CHÚ Ý: Nếu bạn nói Tiếng Việt, có các dịch vụ hỗ trợ ngôn ngữ miễn phí dành cho bạn. Gọi số 1-800-332-6501 (TTY: 711).

**Pennsylvania Dutch**: Wann du Deitsch (Pennsylvania German / Dutch) schwetzscht, kannscht du mitaus Koschte ebbergricke, ass dihr helft mit die englisch Schprooch. Ruf selli Nummer uff: Call 1-800-332-6501 (TTY: 711).

**Lao**: ໂປດຊາບ: ຖ້າວ່າ ທ່ານເວົ້າພາສາ ລາວ, ການບໍລິການຊ່ວຍເຫຼືອດ້ານພາສາ,ໂດຍບໍ່ເສັງຄ່າ, ແມ່ນມີພ້ອມໃຫ້ທ່ານ. ໂທຣ 1-800-332-6501 (TTY: 711).