Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope	
Iron Agents	MP-RX-FP-44-23	☒ MMM MA	☒ MMM Multihealth

Service Category

☐ Anesthesia
☐ Surgery
☐ Radiology Procedures
☐ Pathology and Laboratory Procedures
☐ Medicine Services and Procedures
☐ Evaluation and Management Services
☐ DME/Prosthetics or Supplies
☒ Part B Drugs

Service Description

This document addresses the use of Ferumoxytol (Feraheme), Ferric carboxymaltose (Injectafer), Sodium ferric gluconate/sucrose complex (Ferrlecit), Iron dextran (Infed), Ferric carboxymaltose (Injectafer), Ferric derisomaltose (Monoferric), Ferric pyrophosphate citrate (Triferic, Triferic AVNU), Iron sucrose (Venofer) , a drug approved by the Food and Drug Administration (FDA) for the treatment of iron deficiency anemia (IDA).

Background Information

This document addresses the use of injectable agents for the treatment of iron deficiency anemia (IDA). Agents addressed in this document include:

- Feraheme (ferumoxytol)
- Ferrlecit (sodium ferric gluconate/sucrose complex)
- Infed (iron dextran)
- Injectafer (ferric carboxymaltose)
- Monoferric (ferric derisomaltose)
- Triferic, Triferic AVNU (ferric pyrophosphate citrate)
- Venofer (iron sucrose)

Iron is a mineral in the body that is an essential component for blood production, enabling them to carry oxygen throughout the body. The majority of body iron are found in circulating red blood cells called hemoglobin, while the remaining is stored as ferritin or bound to myoglobin in muscle cells. Individuals with iron deficiency anemia may have mild to severe symptoms, ranging from fatigue, shortness of breath, and chest pain to heart failure and developmental delays in children (NHLBI 2019).

The causes of iron deficiency anemia are numerous, including gastrointestinal bleeding or other blood loss, chronic kidney disease, celiac disease, multiple blood donations, and cancer or chemotherapy-related etiologies. Diagnosis of IDA is typically confirmed by evaluating levels of serum ferritin, transferrin saturation (TSAT), absence of stainable iron in the bone marrow, or resolution of anemia upon iron administration (Auerbach 2020).

While the 2012 Kidney Disease Improving Global Outcomes (KDIGO) guidelines for anemia in chronic kidney disease do not provide any guidance on preference of available IV iron agents over another, they do suggest that a trial oral iron for 1 to 3 months can be appropriate for individuals with IDA prior to initiating IV iron. The National Comprehensive Cancer Network (NCCN) guidelines for Hematopoietic Growth Factors provides a category 2A

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recommendation for use of Feraheme, Ferrlecit, Infed (IV only; IM not recommended), Injectafer, Venofer, and Monoferric for the management of cancer- and chemotherapy-induced anemia. NCCN also suggests that a trial of oral iron for at least 4 weeks can be appropriate prior to initiating IV iron.

Both Feraheme and Infed have black box warnings for fatal and serious hypersensitivity reactions including anaphylaxis, and as such, the administration of which should only occur when personnel and therapies are immediately available for the treatment of anaphylaxis and other hypersensitivity reactions.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS	Description
J1443	Injection, ferric pyrophosphate citrate solution, 0.1 mg of iron [Triferic]
J1445	Injection, ferric pyrophosphate citrate solution (Triferic AVNU), 0.1 mg of iron
J1437	Injection, ferric derisomaltose, 10 mg [Monoferric]
Q0138	Injection, ferumoxytol, for treatment of iron deficiency anemia, 1 mg (for non-ESRD on dialysis) [Feraheme]
J2916	Injection, sodium ferric gluconate complex in sucrose injection, 12.5 mg [Ferrlecit]
J1750	Injection, iron dextran, 50 mg [Infed]
J1756	Injection, iron sucrose, 1 mg [Venofer]
J1439	Injection, ferric carboxymaltose, 1 mg [Injectafer]

ICD-10	Description
D50.0-D50.9	Iron deficiency anemia
D63.0-D63.8	Anemia in chronic diseases classified elsewhere
D64.81	Anemia due to antineoplastic chemotherapy
E61.1	Iron deficiency anemia
K50.00-K50.919	Crohn's disease [regional enteritis]
K90.0-K90.9	Celiac disease
N18.1-N18.5	Chronic kidney disease, stages I-V
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

Medical Necessity Guidelines

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Feraheme (ferumoxytol), Ferrlecit (sodium ferric gluconate/sucrose complex), Infed (iron dextran), Injectafer (ferric carboxymaltose), Venofer (iron sucrose)

A. Prescriber Specialties: N/A

B. Criteria For Initial Approval

I. Individual has a diagnosis of chronic kidney disease (CKD); **AND**
   A. Individual is dialysis dependent; **AND**
   B. Individual has iron deficiency anemia (IDA);

OR

II. Individual has a diagnosis of iron deficiency anemia (IDA) or iron deficiency; **AND**
III. Individual is non-dialysis dependent; **AND**
IV. Diagnosis is confirmed by one of the following:
   A. For IDA associated with CKD or inflammatory conditions (for example, inflammatory bowel disease [IBD], heart failure), individual meets one of the following within the last four (4) weeks (De Franceschi 2017):
      1. Serum ferritin levels less than 100 ng/mL; **OR**
      2. TSAT levels less than 20%; **OR**
      3. Serum ferritin is less than or equal to 500 ng/mL and TSAT is less than or equal to 30% (KDIGO 2012); **OR**
      4. Bone marrow demonstrates inadequate iron stores; **OR**
      5. Hemoglobin (HGB) less than 13 g/dl (less than 130 g/l) in males or less than 12 g/dl (less than 120 g/l) in females and TSAT 30% or less and ferritin 500ng/ml or less (500 µg/l or less) (Ko 2020); **OR**
   B. For IDA associated with cancer/chemotherapy or non-inflammatory conditions (for example, blood loss, malabsorption, malnutrition), individual meets one of the following within the last four (4) weeks (NCCN 2021, De Franceschi 2017):
      1. Serum ferritin levels less than 30 ng/mL; **OR**
      2. TSAT levels less than 20%; **OR**
      3. Bone marrow demonstrates inadequate iron stores; **AND**
V. Individual has had a four (4) week trial of and inadequate response, or intolerance to oral iron supplementation (NCCN 2020, KDIGO 2012); **OR**
VI. Individual is unable to use oral iron supplementation for one of the following reasons:
   A. Malabsorption conditions; **OR**
   B. Gastric Surgery (DeFlipp 2013);

OR

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VII. Individual has iron deficiency anemia in pregnancy; **AND**
VIII. Diagnosis is confirmed by one of the following:
   A. Serum ferritin levels less than 30 ng/mL; **OR**
   B. TSAT levels less than 20%; **OR**
   C. Bone marrow demonstrates inadequate iron stores; **AND**
IX. Individual is past 14 weeks of pregnancy and has had a four (4) week trial of and inadequate response, or intolerance to oral iron supplementation (Muñoz 2017); **OR**
X. Individual is past 14 weeks of pregnancy and individual is unable to use oral iron supplementation due to malabsorptive conditions or gastric surgery (Muñoz 2017, DeFlipp 2013); **OR**
XI. Individual is past 14 weeks of pregnancy and diagnosed with severe iron deficiency anemia, defined as Hemoglobin (HGB) less than 8 g/dL; **OR**
XII. Individual is past 34 weeks of pregnancy

OR

XIII. ONLY for INFED (Iron dextran): Individual is diagnosed with iron deficiency due to blood loss; **AND**
XIV. Diagnosis is confirmed by one of the following:
   A. Serum ferritin levels less than 100 ng/mL; **OR**
   B. TSAT levels less than 20%; **OR**
   C. Serum ferritin is less than or equal to 500 ng/mL ***and*** TSAT is less than or equal to 30% (KDIGO 2012); **OR**
   D. Bone marrow demonstrates inadequate iron stores.

OR

XV. ONLY for Injectafer (ferric carboxymaltose): Individual is diagnosed with iron deficiency in adult patients with heart failure with New York Heart Association class II/III; **AND**
XVI. Individual is using to improve exercise capacity; **AND**
XVII. Diagnosis is confirmed by one of the following (Heidenreich 2022):
XVIII. Serum ferritin levels less than 100 µg/L; **OR**
XIX. TSAT levels less than 20% and ferritin level 100 to 300 µg/L.

C. Criteria For Continuation of Therapy: N/A

D. Authorization Duration (dialysis-dependent use excluded): 6 months

E. Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

Feraheme (ferumoxytol), Ferrlecit (sodium ferric gluconate/sucrose complex), Infed (iron dextran), Injectafer (ferric carboxymaltose), or Venofer (iron sucrose) may not be approved when the above criteria are not met and for all other indications.

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Monoferric (ferric derisomaltose)

A. Prescriber Specialties: N/A

B. Criteria For Initial Approval

I. Individual has a diagnosis of iron deficiency anemia (IDA) or iron deficiency; **AND**
II. Individual is non-dialysis dependent; **AND**
III. Diagnosis is confirmed by one of the following:
  A. For IDA associated with CKD or inflammatory conditions (for example, inflammatory bowel disease [IBD], heart failure), individual meets one of the following within the last four (4) weeks (De Franceschi 2017):
    1. Serum ferritin levels less than 100 ng/mL; **OR**
    2. TSAT levels less than 20%; **OR**
    3. Serum ferritin is less than or equal to 500 ng/mL and TSAT is less than or equal to 30% (KDIGO 2012); **OR**
    4. Bone marrow demonstrates inadequate iron stores; **OR**
    5. Hemoglobin (HGB) less than 13 g/dl (less than 130 g/l) in males or less than 12 g/dl (less than 120 g/l) in females and TSAT 30% or less and ferritin 500ng/ml or less (500 µg/l or less) (Ko 2020); **OR**
  B. For IDA associated with cancer/chemotherapy or non-inflammatory conditions (for example, blood loss, malabsorption, malnutrition), individual meets one of the following within the last four (4) weeks (NCCN 2021, De Franceschi 2017):
    1. Serum ferritin levels less than 30 ng/mL; **OR**
    2. TSAT levels less than 20%; **OR**
    3. Bone marrow demonstrates inadequate iron stores; **AND**
IV. Individual has had a four (4) week trial of and inadequate response, or intolerance to oral iron supplementation (NCCN 2020, KDIGO 2012); **OR**
V. Individual is unable to use oral iron supplementation for one of the following reasons:
  A. Malabsorption conditions; **OR**
  B. Gastric Surgery (DeFlipp 2013);

C. Criteria For Continuation of Therapy: N/A

D. Authorization Duration: 6 months

E. Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

I. Individual has hemodialysis dependent chronic kidney disease (CKD); **OR**
II. When the above criteria are not met and for all other indications.

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Triferic/Triferic AVNU (ferric pyrophosphate citrate)

A. Prescriber Specialties: N/A

B. Criteria For Initial Approval

i. Individual has a diagnosis of chronic kidney disease (CKD); **AND**
ii. Individual is hemodialysis dependent; **AND**
iii. Individual has iron deficiency anemia (IDA).

C. Criteria For Continuation of Therapy: N/A

D. Authorization Duration: 6 months

E. Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

I. Peritoneal dialysis; **OR**
II. When the above criteria are not met and for all other indications.

Summary of FDA-approved and NCCN 2A recommended indications for agents for Iron Deficiency Anemia (IDA):

Agent	Route	Oral iron intolerant or unresponsive IDA	CKD	Dialysis-dependent CKD only	NCCN
Feraheme (ferumoxytol)	IV	X	X		X
Ferrlecit (sodium ferric gluconate/sucrose complex)	IV			X*	X
Infed (iron dextran)	IV, IM	X*			X (IV only)
Injectafer (ferric carboxymaltose)	IV	X	X		X
Monoferric (ferric carboxymaltose)	IV	X	X		X
Triferic, Triferic AVNU (ferric pyrophosphate citrate)	IV			X	
Venofer (iron sucrose)	IV		X*		X

*Includes FDA-approved pediatric indication.

Note: When an IDA agent is deemed approvable based on the clinical criteria above, the benefit plan may have additional criteria requiring the use of a preferred agent or agents.

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Limits or Restrictions

A. Therapeutic Alternatives

This medical policy may be subject to Step Therapy. Please refer to the document published on the MMM Website: https://www.mmm-pr.com/planes-medicos/formulario-medicamentos

B. Quantity Limitations

Iron Deficiency Anemia Agents Quantity Limits

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

Drug	Limit
Feraheme (ferumoxytol) 510 mg/17 mL vial*	2 vials per 6 days‡
Ferrlecit (sodium ferric gluconate/sucrose complex) 62.5 mg/5 mL vial*	16 vials per 8 weeksΔ
Injectafer (ferric carboxymaltose) 750 mg/15 mL vial*	2 vials per 14 days‡
Injectafer (ferric carboxymaltose) 100mg/2ml vial*	7 vials per 7 days
Injectafer (ferric carboxymaltose) 1000 mg/20 mL vial*	1 vial per 7 days
Monoferric (ferric derisomaltose) 100 mg/mL vial	4 vials per day
Monoferric (ferric derisomaltose) 500 mg/5 mL vial	1 vial per day
Monoferric (ferric derisomaltose) 1000 mg/10 mL vial	1 vial per day‡
Venofer (iron sucrose) 50 mg/2.5 mL vial*	6 vials per 12 weeks
Venofer (iron sucrose) 100 mg/5 mL vial*	3 vials per 12 weeks
Venofer (iron sucrose) 200 mg/10 mL vial*	5 vials per 14 days‡
Override Criteria	
*Use in dialysis-dependent individuals excluded from quantity limits.	

‡ Limit represents FDA-approved maximum dose recommendations per course of therapy (excluding dialysis-dependent diagnosis).
ΔLimit according to NCCN guidelines for hematopoietic growth factors (v4.2021).

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Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

Policy History

Revision Type	Summary of Changes	P&T Approval Date	MPCC Approval Date
Annual Review 07/15/2024	Add hemoglobin in diagnosis, edit oral iron requirement, update Infed criteria to include iron deficiency from blood loss, Add Injectafer criteria related to heart failure, increase approval length to 6 monyhs; Add iron deficiency clarification, add oral iron exception requirements to anemia in pregnancy, clarify blood loss iron deficiency for Infed; Coding Reviewed: Add ICD-10-CM E61.1	2/24/2025	3/6/2025
Policy Inception 08/18/2023	Elevance Health's Medical Policy adoption.	N/A	11/30/2023