Clinical Policy: Ferric Carboxymaltose (Injectafer)

Reference Number: LA.PHAR.234
Effective Date: 09.18.21
Last Review Date: ~~06.14.23~~04.29.24 Coding Implications
Line of Business: Medicaid Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

****Please note: This policy is for medical benefit****

Description
Ferric carboxymaltose (Injectafer®) injection is an iron replacement product.

FDA Approved Indication(s)
Injectafer is indicated for treatment of ~~iron deficiency anemia (IDA) in:~~:

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

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

It is the policy of Louisiana Healthcare Connections that Injectafer is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Iron Deficiency Anemia with Chronic Kidney Disease (must meet all):

1. Diagnosis of IDA and CKD;
2. IDA is confirmed by either of the following:
   a. Transferrin saturation (TSAT) ≤ 30%;
   b. Serum ferritin ≤ 500 ng/mL;
3. If CKD does not require hemodialysis or peritoneal dialysis, oral iron therapy is not optimal due to any of the following:
   a. TSAT < 12%;
   b. Hgb < 7 g/dL;
   c. Symptomatic anemia;
   d. Severe or ongoing blood loss;
   e. Oral iron intolerance;
   f. Unable to achieve therapeutic targets with oral iron;
   g. Co-existing condition that may be refractory to oral iron therapy;
4. Member meets ~~one~~both of the following (a~~,~~ and b~~, or c~~):
   ~~a. Age < 2 years;~~

~~b.~~ Failure of both of the following ~~(i and ii):~~
~~i. If age ≥ 6 years,~~, unless clinically significant adverse effects are experienced or both are contraindicated: **Ferrlecit**®~~;~~
~~ii.~~a. ~~If age ≥ 2 years,~~ ® and **Venofer**®;
~~c. Member~~If member has ~~intolerance or contraindication to both Ferrlecit and Venofer, and one of the following (i or ii):~~
~~i. Age < 18 years;~~
~~ii.~~b. ~~Age ≥ 18 years and~~satisfied criteria 4a above, failure of **generic Feraheme**®, unless contraindicated or clinically significant adverse effects are experienced;

5. Dose does not exceed two 750 mg elemental iron infusions/injections or a single 1,000 mg elemental iron infusion/injection.

Approval duration: 3 months

B. Iron Deficiency Anemia without Chronic Kidney Disease (must meet all):

1. Diagnosis of IDA confirmed by any of the following:
   a. Serum ferritin < 15 ng/mL or < 30 ng/mL if pregnant;
   b. Serum ferritin ≤ 41 ng/mL and Hgb < 12 g/dL (women)/< 13 g/dL (men);
   c. TSAT < 20%;
   d. Absence of stainable iron in bone marrow;
   e. Increased soluble transferring receptor (sTfR) or sTfR-ferritin index;
   f. Increased erythrocyte protoporphyrin level;
2. Oral iron therapy is not optimal due to any of the following:
   a. TSAT < 12%;
   b. Hgb < 7 g/dL;
   c. Symptomatic anemia;
   d. Severe or ongoing blood loss;
   e. Oral iron intolerance;
   f. Unable to achieve therapeutic targets with oral iron;
   g. Co-existing condition that may be refractory to oral iron therapy;
3. At the time of the request, member does not have CKD;
4. Member meets ~~one~~both of the following (a~~,~~ and b~~, or c~~):
   ~~a. Age < 2 years and failure of Infed~~®~~;~~
   ~~b.~~ Failure of two of the following~~:~~
   ~~a. Infed;~~
   ~~b. If age ≥ 6 years,~~, unless clinically significant adverse effects are experienced or all are contraindicated: **Ferrlecit**~~;~~
   ~~c. If age ≥ 2 years, Venofer;~~
   ~~c.~~a. ~~Member has intolerance or contraindication to all preferred injectable agents (e.g. Ferrlecit, Infed,~~ **Infed**®, or **Venofer**~~), and one of the following (i or ii):~~;
   ~~a. Age < 18 years;~~
   ~~ii.~~b. ~~Age ≥ 18 years and~~If member has satisfied criteria 4a above, failure of **generic Feraheme**, unless contraindicated or clinically significant adverse effects are experienced~~;~~

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5. Dose does not exceed two 750 mg elemental iron infusions/injections or a single 1,000 mg elemental iron infusion/injection.

Approval duration: 3 months

C. Iron Deficiency with Heart Failure (must meet all):

1. Diagnosis of iron deficiency confirmed by ~~any~~either of the following~~:~~ (a or b):
   a. Serum ferritin level < 100 ng/mL;
   b. Serum ferritin level between 100 to 300 ng/mL and TSAT < 20%;
2. Member meets all of the following~~:~~ (a, b, c, and d):
   a. Hb < 15 g/dL;
   b. LVEF ≤ 45%;
   c. ~~New York Heart Association~~NYHA class II or ~~II *(Appendix D)*;~~III;
   d. Age ≥ 18 years;
3. Dose does not exceed 1,000 mg elemental iron per infusion/injection.

Approval duration: 3 months

~~**D.**~~ **Other diagnoses/~~-~~indications** (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: LA.PMN.53 for Medicaid.

II. Continued Therapy

A. Iron Deficiency Anemia with Chronic Kidney Disease (must meet all):

1. Currently receiving medication via Louisiana Healthcare Connections benefit or member has previously met initial approval criteria;
2. Documentation of one of the following laboratory results measured since the last IV iron administration (a or b):
   a. TSAT ≤ 30%;
   b. Serum ferritin ≤ 500 ng/mL;
3. Member meets ~~one~~both of the following (a~~,~~ and b~~, or c~~):

~~a. Age < 2 years;~~

~~b.~~ Failure of both of the following ~~(i and ii):~~

~~i. If age ≥ 6 years,~~, unless clinically significant adverse effects are experienced or both are contraindicated: **Ferrlecit**®~~;~~

~~ii.~~a.~~If age ≥ 2 years,~~ and **Venofer**®~~;~~;

~~c. Member~~If member has ~~intolerance or contraindication to both Ferrlecit and Venofer, and one of the following (i or ii):~~

~~i. Age < 18 years;~~

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~~ii.~~b. ~~Age ≥ 18 years and~~satisfied criteria 3a above, failure of **generic Feraheme®**~~,~~, unless contraindicated or clinically significant adverse effects are experienced;

4. If request is for a dose increase, new dose does not exceed two 750 mg elemental iron infusions/injections or a single 1,000 mg elemental iron infusion/injection.

Approval duration: 3 ~~months~~month

B. Iron Deficiency Anemia without Chronic Kidney Disease (must meet all):

1. Currently receiving medication via Louisiana Healthcare Connections benefit or member has previously met initial approval criteria;
2. Documentation of one of the following laboratory results measured since the last IV iron administration (a, b, c, d, e, or f):
   a. Serum ferritin < 15 ng/mL or < 30 ng/mL if pregnant;
   b. Serum ferritin ≤ 41 ng/mL and Hb < 12 g/dL (women)/< 13 g/dL (men);
   c. TSAT < 20%;
   d. Absence of stainable iron in bone marrow;
   e. Increased sTfR or sTfR-ferritin index;
   f. Increased erythrocyte protoporphyrin level;
3. At the time of the request, member does not have CKD;
4. ~~Member meets one~~both of the following (a~~, b, or c):~~

~~a.~~4. ~~Age < 2 years~~ and ~~failure of Infed;~~b):

~~b. Failure of two of the following:~~

~~a. Infed;~~

~~b. If age ≥ 6 years.~~, unless clinically significant adverse effects are experienced or all are contraindicated: **Ferrlecit~~;~~**

~~iii.~~a. ~~If age ≥ 2 years,~~ **, Infed**, or **Venofer**;

~~c. Member has intolerance or contraindication to all preferred injectable agents (e.g. Ferrlecit, Infed, or Venofer), and one of the following (i or ii):~~

~~a. Age < 18 years;~~

~~ii.~~b. ~~Age ≥ 18 years and failure of~~If member has satisfied criteria 4a above, failure of **generic Feraheme**, unless contraindicated or clinically significant adverse effects are experienced;

5. If request is for a dose increase, new dose does not exceed two 750 mg elemental iron infusions/injections or a single 1,000 mg elemental iron infusion/injection.

Approval duration: 3 months

C. Iron Deficiency with Heart Failure (must meet all):

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations *(refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B)*;

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2. Documentation of one of the following laboratory results measured since the last IV iron administration (a or b):
   a. Serum ferritin <100 ng/mL;
   b. Serum ferritin 100 to 300 ng/mL with transferrin saturation < 20~~%~~%;
3. If request is for a dose increase, new dose does not exceed a single 1,000 mg elemental iron infusion/injection.

Approval duration: 3 months

D. Other diagnoses/indications (must meet 1 or 2):
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: LA.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – LA.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CKD: chronic kidney disease
ESA: erythropoiesis stimulating agent
Hb: hemoglobin
~~NYHA: New York Heart Association~~
IDA: iron deficiency anemia
~~TSAT: transferrin saturation~~
LVEF: left ventricular ejection fraction
NYHA: New York Heart Association
TSAT: transferrin saturation
sTfR: soluble transferring receptor

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Examples of OTC Oral Iron Formulations*		
Ferrous fumarate (Ferretts, Ferrimin 150)	Varies	
Ferrous gluconate (Ferate)		
Ferrous sulfate (BProtected Pedia Iron, Fer-In-Sol, FeroSul, Iron Supplement, Iron Supplement Childrens, Slow Fe, Slow Iron)		

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Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Polysaccharide-iron complex (EZFE 200, Ferrex 150, Ferrix x-150, IFerex 150, NovaFerrum 125, NovaFerrum, NovaFerrum Pediatric Drops, Nu-Iron, Poly-Iron 150)		
Injectable iron agents		
Sodium ferric gluconate (Ferrlecit)	Varies	
Infed (iron dextran)		
Venofer (iron sucrose)		
Ferumoxytol (Feraheme ~~(ferumoxytol)~~)		

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
**Oral formulations include elixirs, liquids, solutions, syrups, capsules, and tablets - including delayed/extended-release tablets.*

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): Hypersensitivity to Injectafer or any of its inactive components.
- Boxed warning(s): None reported.

V. Dosage and Administration

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Indication	Dosing Regimen	Maximum Dose
~~IDA with non-dialysis dependent CKD (adults)~~IDA	≥ 50kg (110lb): two 750 mg doses by IV infusion separated by at least 7 days for a cumulative dose of 1,500 mg per course. In adults: Alternatively, a single-dose treatment course may be administered as 15 mg/kg to a maximum of 1,000 mg. < 50kg (110lb): two doses by IV infusion separated by at least 7 days as 15 mg/kg body weight.	Two dose treatment course: 750 mg per dose (up to 1,500 mg) Single dose treatment course: 1,000 mg Treatment may be repeated
~~IDA with intolerance to oral iron or unsatisfactory response to oral iron (adults and pediatric patients ≥ 1 year old)~~	~~≥ 50kg (110lb): two 750 mg doses by IV infusion separated by at least 7 days for a cumulative dose of 1,500 mg per course.~~ ~~< 50kg (110lb): two doses by IV infusion separated by at least 7 days as 15 mg/kg body weight.~~	~~See dosing regimen~~
Iron deficiency with heart failure and	≥< 70 kg (154lb): Hb < 10 g/dL: 1,000 mg on day 1, then 500 mg on week 6	See dosing regimen

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Indication	Dosing Regimen	Maximum Dose
NYHA Class II/III (adults)	Hb 10 to 14 g/dL: 1,000 mg on day 1 Hb > 14 to < 15 g/dL: 500 mg on day 1 ~~<~~= 70 kg (154lb): Hb < 10 g/dL: 1,000 mg on day 1, then 1,000 mg on week 6 Hb 10 to 14 g/dL: 1,000 mg on day 1, then 500 mg on week 6 Hb > 14 to < 15 g/dL: 500 mg on day 1 Maintenance dose: 500 mg at 12, 24 and 36 weeks.	

VI. Product Availability

Intravenous solution single-dose vial: 100 mg/2 mL, 750 mg/15 mL, 1,000 mg/20 mL

VII. References

1. Injectafer prescribing information. Shirley, NY: American Regent, Inc.; May 2023. Available from https://injectafer.com/. Accessed ~~June~~October 12, 2023.
2. KDIGO 2012 clinical practice guideline for evaluation and management of chronic kidney disease. *Kidney International Supplements.* January 2013; 3(1): 1-136.
3. KDIGO 2012 clinical practice guideline for anemia in chronic kidney disease. *Kidney International Supplements.* August 2012; 2(4): 279-331.
4. Babitt JL, Eisenga MF, Haase VH, et al. Controversies in optimal anemia management: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Conference. Kidney Int. 2021;99(6):1280-1295.
5. Camaschella C. Iron-Deficiency Anemia. *N Engl J Med.* 2015; 372: 1832-43. DOI: 10.1056/NEJMra1401038.
6. Short MW, Domagalski JE. Iron Deficiency Anemia: Evaluation and Management. *Am Fam Physician.* 2013; 87(2): 98-104. http://www.aafp.org/afp/2013/0115/p98.pdf
7. Oral iron monographs. In: UpToDate (Lexicomp), Waltham, MA: Wolters Kluwer Health. Updated periodically. Accessed November ~~20, 2022~~4, 2023.
8. 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.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-

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date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J1439	Injection, ferric carboxymaltose, 1 mg

Reviews, Revisions, and Approvals	Date	LDH Approval Date
Converted corporate to local policy.	06.2021	09.18.21
Template changes applied to other diagnoses/indications and continued therapy section. Added updated vial strength of 100 mg/2 mL; FDA-approved age expansion was updated to reflect approval for pediatric patients 1 year of age and older who have either intolerance to oral iron or have had an unsatisfactory response to oral iron; references reviewed and updated. Updated initial criteria to require failure of the following with associated age considerations: for IDA and CKD Ferrlecit and Venofer; for IDA without CKD two of Ferrlecit, Infed, or Venofer; additionally, added redirection to Feraheme in a step-wise fashion if member has intolerance or contraindication to all preferred injectable agents. Added blurb this policy is for medical benefit only. Updated FDA Approved Indications(s) section to include iron deficiency with heart failure per updated prescribing information; added to Section I, II, and IV for new indication. Per health plan request and SDC, for IDA with and without CKD, added redirections from initial approval criteria to continued therapy.	06.14.23	01.03.24
Annual review; revised to template redirection language and simplified to remove redirection by age; revised redirection to Feraheme to instead require generic Feraheme; corrected NYHA class for heart failure indication	04.29.24	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. LHCC makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved.

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The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable LHCC administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. LHCC retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom LHCC has no control or right of control. Providers are not agents or employees of LHCC.

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