Clinical Policy Title:	ferric carboxymaltose
Policy Number:	RxA.394
Drug(s) Applied:	Injectafer®
Original Policy Date:	03/06/2020
Last Review Date:	09/14/2021
Line of Business Policy Applies to:	All lines of business

Background

Ferric carboxymaltose (Injectafer®) is an iron replacement product indicated for treatment of iron deficiency anemia (IDA) in adult patients who have:

- Intolerance to oral iron or have had unsatisfactory response to oral iron; or
- Non-dialysis dependent chronic kidney disease (CKD).

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
ferric carboxymaltose (Injectafer®)	IDA with or without non-dialysis dependent CKD (adults)	≥ 50kg (110lb): Two 750 mg doses intravenously separated by at least 7 days for a cumulative dose of 1500 mg of iron per course. Alternatively, Injectafer® 15 mg/kg to a maximum of 1,000 mg may be administered as a single dose treatment course. < 50kg (110lb): Two doses separated by at least 7 days as 15 mg/kg body weight intravenously. Treatment may be repeated if iron deficiency anemia reoccurs.	≥ 50kg (110lb): 15 mg/kg/dose IV (Max: 1,000 mg/dose) when given as a single-dose; 750 mg IV when given as a 2-dose course (Max: 1,500 mg total cumulative dose). < 50kg (110lb): 15 mg/kg/dose for 2 doses (Max: 30 mg/kg total cumulative dose).

Dosage Forms

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

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain

coverage.

I. Initial Approval Criteria

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

1. Diagnosis of IDA with CKD;
2. Age ≥ 18 years;
3. IDA is confirmed by either of the following:
   a. Transferrin saturation (TSAT) ≤ 30%;
   b. Serum ferritin ≤ 500 ng/mL;
4. If CKD does not require hemodialysis or peritoneal dialysis, oral iron therapy is not optimal due to any of the following:
   a. Hgb < 7 g/dL;
   b. TSAT < 12%;
   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;
5. Dose does not exceed 750 mg elemental iron per infusion/injection.

Approval duration
Commercial: 3 months
Medicaid: 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. Age ≥ 18 years;
4. At the time of the request, member does not have CKD;
5. Dose does not exceed 750 mg elemental iron per infusion/injection.

Approval duration
Commercial: 3 months
Medicaid: 3 months

II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to the therapy;
3. Documentation of one of the following laboratory results measured since the last intravenous iron administration:
   a. TSAT ≤ 30%;
   b. Serum ferritin ≤ 500 ng/mL;
4. If request is for a dose increase, new dose not exceed 750 mg elemental iron per infusion/injection.

Approval duration
Commercial: 3 months
Medicaid: 3 months

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

1. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to the therapy;
3. Documentation of one of the following laboratory results measured since the last intravenous iron administration:
   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;
4. At the time of the request, member does not have CKD;
5. If request is for a dose increase, new dose does not exceed 750 mg elemental iron per infusion/injection.

Approval duration
Commercial: 3 months
Medicaid: 3 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
CKD: Chronic kidney disease
ESA: Erythropoiesis stimulating agent
Hb: Hemoglobin
IDA: Iron deficiency anemia
sTfR: Soluble transferring receptor
TSAT: Transferrin saturation
FDA: Food and Drug Administration

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/Maximum Dose

Examples of OTC Oral Iron Formulations*	
Ferrous fumarate (Ferretts®, Ferrimin 150, Hemocyte®)	Varies
Ferrous gluconate (Ferate)	
Ferrous sulfate (B Protected™ Pedia Iron, Fer-In-Sol®, FeroSul®, FerrouSul™, Iron Supplement Children Slow Fe®, Slow Iron®)	
Polysaccharide-iron complex (EZFE 200, Ferrex™ 150, Ferrix™ x150, Myferon™ 150, NovaFerrum® 125, NovaFerrum® 50, NovaFerrum® Pediatric Drops, Nu-Iron®, Poly-Iron 150)	

Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both brand and generic; Brand name® when the drug is available by brand only and generic when the drug is available by generic only.
*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.

APPENDIX D: General Information

- Hypersensitivity Reactions: Observe for signs and symptoms of hypersensitivity during and after Injectafer® administration for at least 30 minutes and until clinically stable following completion of each administration.
- Symptomatic Hypophosphatemia: Monitor serum phosphate levels in patients at risk for low serum phosphate who require a repeat course of treatment.
- Hypertension: Monitor patients closely for signs and symptoms of hypertension following each Injectafer® administration.

References

1. Injectafer® prescribing information. Shirley, NY: American Regent, Inc.; April 2021. Available from https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=517b4a19-45b3-4286-9f6a-ced4e10447de&type=display#section-3 . Accessed June 02, 2021.
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. Camaschella C. Iron-Deficiency Anemia. N Engl J Med. 2015; 372: 1832-43. DOI: 10.1056/NEJMra1401038.
5. 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
6. Oral iron monographs. In: UpToDate (Lexicomp), Waltham, MA: Walters Kluwer Health; 2018. Available at www.uptodate.com. Accessed June 02, 2021

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: 1. Clinical Policy Title was updated. 2. Drug(s) Applied was updated. 3. Line of Business Policy Applies to was updated. 4. Continued Therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..." 5. Commercial approval duration and Medicaid approval duration updated. 6. Updated Dosing Information to specify maximum dose and included “Treatment may be repeated if iron deficiency anemia reoccurs” 7. Updated dosage form to “Intravenous solution: 750 mg iron/15 mL single- dose vial” 8. References were updated.	07/14/2020	09/14/2020
Policy was reviewed: 1. Dosing Information dosing regimen was updated to include “Alternatively, Injectafer® 15 mg/kg to a maximum of 1,000 mg…” 2. Dosing Information maximum dose was updated to include “15 mg/kg/dose IV (Max: 1,000 mg/dose) when given as a single-dose…” 3. Dosage Forms was updated to include “1,000 mg iron/20 mL single-dose vial…” 4. Statement about provider sample ‘‘The provision of provider samples does not guarantee coverage…” was added to Clinical Policy. 5. Initial Approval Criteria I.A.2 was updated to include “Age ≥ 18 years…” 6. Initial Approval Criteria I.B.3 was updated to include “Age ≥ 18 years…” 7. Continuation Therapy Approval Criteria II.A.2 was updated to include “Member is responding positively to the therapy …” 8. Continued Therapy Approval Criteria II.B.2 was updated to include “Member is responding positively to the therapy…” 9. Appendix A was updated to include abbreviation FDA. 10. Statement about drug listing format in Appendix B is rephrased to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic only".	06/02/2021	09/14/2021

11. Appendix D: General Information was updated to include “Hypersensitivity Reactions: Observe for signs and symptoms…” 12. References were reviewed and updated.		