Clinical Policy: Iron Sucrose (Venofer)

Reference Number: CP.PHAR.167
Effective Date: 03.01.16
Last Review Date: 02.21
Line of Business: HIM, Medicaid

Coding Implications
Revision Log

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

Description

Iron sucrose (Venofer®) injection is an iron replacement product.

FDA Approved Indication(s)

Venofer is indicated for the treatment of iron deficiency anemia (IDA) in patients with chronic kidney disease (CKD).

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 health plans affiliated with Centene Corporation® that Venofer 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. Dose does not exceed 500 mg elemental iron per injection.

Approval duration: 3 months

B. Iron Deficiency Anemia without Chronic Kidney Disease (off-label) (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. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration 3 months

C. Other diagnoses/indications:

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid and HIM.PA.154 for health insurance marketplace.

II. Continued Approval Criteria

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

1. Currently receiving the medication via Centene benefit or member has previously met all initial approval criteria;
2. Documentation of one of the following laboratory results measured since the last IV iron administration:
   a. TSAT ≤ 30%;
   b. Serum ferritin ≤ 500 ng/mL;
3. If request is for a dose increase, new dose does not exceed 500 mg elemental iron per injection.

Approval duration 3 months

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

1. Currently receiving the medication via Centene benefit or member has previously met all initial approval criteria;
2. Documentation of one of the following laboratory results measured since the last IV 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;
3. At the time of the request, member does not have CKD;
4. If request is for a dose increase, new dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration 3 months

C. Other diagnoses/indications (must meet 1 or 2):
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid and HIM.PA.154 for health insurance marketplace.

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 – HIM.PA.154 for health insurance marketplace and CP.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
IDA: iron deficiency anemia
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, Hemocyte)	Varies	
Ferrous gluconate (Ferate)		
Ferrous sulfate (BProtected Pedia Iron, Fer-In-Sol, FeroSul, FerrouSul, Iron Supplement, Iron Supplement Childrens, Slow Fe, Slow Iron)		
Polysaccharide-iron complex (EZFE 200, Ferrex 150, Ferrix x-150, Myferon 150, NovaFerrum 125, NovaFerrum 50, NovaFerrum Pediatric Drops, Nu-Iron, Poly-Iron 150)		

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): Known hypersensitivity to Venofer.
- Boxed warning(s): None reported.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Adults - IDA with CKD: Iron Repletion		
Hemodialysis	100 mg as IV injection or infusion per consecutive HD session.	100 mg per injection/infusion -Treatment course: 1000 mg -Treatment may be repeated
No dialysis	200 mg as IV injection or infusion administered on 5 different occasions over a 14 day period or 500 mg on days 1 and 14.	500 mg per injection/infusion -Treatment course: 1000 mg -Treatment may be repeated
Peritoneal dialysis	3 divided doses, by IV infusion, within a 28 day period: 2 infusions each of 300 mg 14 days apart followed by one 400 mg infusion 14 days later.	400 mg per injection/infusion -Treatment course: 1000 mg -Treatment may be repeated
Children ≥ 2 years - IDA with CKD: Iron Maintenance		
Hemodialysis	0.5 mg/kg slow IV injection or infusion not to exceed 100 mg per dose, every TWO weeks for 12 weeks.	100 mg per injection/infusion -Treatment course: 600 mg -Treatment may be repeated
No dialysis or peritoneal dialysis And receiving erythropoietin therapy	0.5 mg/kg slow IV injection or infusion not to exceed 100 mg per dose, every FOUR weeks for 12 weeks.	100 mg per injection/infusion -Treatment course: 300 mg -Treatment may be repeated

VI. Product Availability

Intravenous solution single-dose vials: 20 mg/mL (2.5 mL, 5mL, 10mL)

VII. References

1. Venofer prescribing information. Shirley, NY: American Regent, Inc.; September 2020. Available from https://www.venofer.com/. Accessed November 18, 2020.
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 November 18, 2020.

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

HCPCS Codes	Description
J1756	Injection, iron sucrose, 1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy developed	01.16	03.16
Under Section I.B, "Iron maintenance treatment in pediatric patients with CKD", the parenthetical, "see mg/kg dosing", is removed from the dosing criteria (even though dosing is weight based) as the intent of the dosing criteria is only to focus on the dose not to exceed.	10/16	
Labeled and off-labeled use, and diagnostic/follow-up tests, are edited for consistency across ferumoxytol, ferric gluconate, iron sucrose, and ferric carboxymaltose policies, and are made broad enough to capture use in adults, children and pregnancy. The criteria also encompass iron maintenance and replenishment. Diagnostic hemoglobin for anemia in men changed from 13.5 to 13 based on WHO criteria. Age and dose are removed. Hypersensitivity removed as a contraindication.	02.17	03.17
1Q18 annual review: - No significant changes - Converted to the new template - Dosing added - References reviewed and updated.	12.01.17	02.18
1Q 2019 annual review; under IDA initial and continuation criteria, a serum ferritin of less than or equal to 500 is edited by deleting the additional requirement of receiving an ESA based on the KDIGO 2012 guidelines which do not include this restriction; under IDA and IDA with CKD continuation criteria, the greater than or equal to 4 week waiting period before retesting after the last IV iron	11.13.18	02.19

Reviews, Revisions, and Approvals	Date	P&T Approval Date
administration is removed per the KDIGO 2012 guidelines which note that only one week need pass before retesting; references reviewed and updated.		
1Q 2020 annual review: no significant changes; added HIM line of business; references reviewed and updated.	11.09.19	02.20
1Q 2021 annual review: for iron deficiency anemia without CKD off-label use, added requirement for provider to submit off-label dosing limits per label or practice guidelines; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	11.18.20	02.21

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. The Health Plan 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. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

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 Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. 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. The Health Plan 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 the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.