Clinical Policy: Ferric Pyrophosphate (Triferic, Triferic Avnu)

Reference Number: CP.PHAR.624
Effective Date: 06.01.23
Last Review Date: 05.24
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

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

Description

Ferric pyrophosphate (Triferic®, Triferic Avnu®) is an iron replacement product.

FDA Approved Indication(s)

Triferic/Triferic Avnu is indicated for the replacement of iron to maintain the hemoglobin in adult patients with hemodialysis-dependent chronic kidney disease (HDD-CKD).

Limitation(s) of use:

- Triferic/Triferic Avnu is not intended for use in patients receiving peritoneal dialysis.
- Triferic/Triferic Avnu has not been studied in patients receiving home hemodialysis.

Policy/Criteria

Provider must submit documentation (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 Triferic/Triferic Avnu is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Iron Replacement Therapy with Hemodialysis-Dependent Chronic Kidney Disease (must meet all)**:**

1. Diagnosis of iron replacement therapy with HDD-CKD;
2. Transferrin saturation (TSAT) ≤ 30%;
3. Serum ferritin ≤ 500 ng/mL;
4. Documentation that Triferic/Triferic Avnu is not used for peritoneal dialysis or home hemodialysis;
5. Failure of Ferrlecit® and Venofer®, unless clinically significant adverse effects are experienced or both are contraindicated;
6. Dose does not exceed 6.75 mg elemental iron per infusion/injection.

Approval duration: 3 months

B. 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 one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business:

CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

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: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Iron Replacement Therapy with Hemodialysis-Dependent Chronic Kidney Disease (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)*;
2. Member is responding positively to therapy as evidenced by, including but not limited to, improvement in any of the following parameters (a, b, or c):
   a. Hgb;
   b. TSAT;
   c. Serum ferritin;
3. Failure of Ferrlecit and Venofer, unless clinically significant adverse effects are experienced or both are contraindicated;
4. If request is for a dose increase, new dose does not exceed 6.75 mg elemental iron per infusion/injection.

Approval duration: 3 months

B. 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 one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
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: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.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 policies – CP.CPA.09 for commercial, 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
HDD-CKD: hemodialysis-dependent chronic kidney disease
Hgb: hemoglobin
TSAT: transferrin saturation

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 for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Sodium ferric gluconate complex in sucrose (Ferrlecit®)	Adults: 125 mg by IV infusion or injection per dialysis session. - May require a cumulative dose of 1000 mg over 8 dialysis sessions. Children age ≥ 6 years: 1.5 mg/kg administered by IV infusion per dialysis session.	125 mg of elemental iron per dose
Venofer® (iron sucrose)	Adults: 100 mg slow intravenous injection or infusion per consecutive hemodialysis session Pediatric patients ≥ 2 years: 0.5 mg/kg slow IV injection or infusion per dose Q 2 weeks for 12 weeks	Adults: 1000 mg total treatment course Pediatric: 100 mg/dose

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.

Appendix C: Contraindications/Boxed Warnings

None reported

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Iron replacement to maintain hemoglobin in patients with hemodialysis-dependent chronic kidney disease	6.75 mg IV administered by slow IV infusion over 3 to 4 hours at each hemodialysis session	Varies Maximum dosage is not defined for hemodialysate use; dose is dependent on dialysate volume used during hemodialysis session.

VI. Product Availability

Drug Name	Availability
Triferic (ferric pyrophosphate solution)	Single dose ampule: 5.44 mg/mL (5 mL)
Triferic (ferric pyrophosphate citrate powder)	Powder packets for injection: 272 mg
Triferic Avnu (ferric pyrophosphate injection)	Injection in single-dose luer lock ampule: 6.75 mg iron (III) per 4.5 mL solution (1.5 mg iron (III) per mL)

VII. References

1. Triferic Prescribing Information. Wixom, MI. Rockwell Medical, Inc.; September 2020. Available from: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=46ec9233-4063-4c48-e054-00144ff8d46c. Accessed February 11, 2024.
2. Triferic Avnu Prescribing Information. Wixom, MI. Rockwell Medical, Inc.; July 2023. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/212860Orig1s001lbl.pdf. Accessed February 11, 2024.
3. KDIGO 2012 clinical practice guideline for anemia in chronic kidney disease. *Kidney International Supplements.* August 2012; 2(4): 279-331.
4. KDIGO 2012 clinical practice guideline for anemia in chronic kidney disease. *Kidney International Supplements.* August 2012; 2(4): 279-331.
5. Aronoff GR, Bennett WM, Blumenthal S, et al; United States Iron Sucrose (Venofer) Clinical Trials Group. Iron sucrose in hemodialysis patients: safety of replacement and maintenance regimens. Kidney Int. 2004 Sep;66(3):1193-8. doi: 10.1111/j.1523-1755.2004.00872.x.
6. Nissenson AR, Lindsay RM, Swan S, et al. Sodium ferric gluconate complex in sucrose is safe and effective in hemodialysis patients: North American Clinical Trial. Am J Kidney Dis. 1999 Mar;33(3):471-82. doi: 10.1016/s0272-6386(99)70184-8.
7. Provenzano R, Schiller B, Rao M, et al. Ferumoxytol as an intravenous iron replacement therapy in hemodialysis patients. Clin J Am Soc Nephrol. 2009 Feb;4(2):386-93. doi: 10.2215/CJN.02840608.
8. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2024. Available at: https://www.clinicalkey.com/pharmacology/. Accessed February 11, 2024.

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
J1443	Injection, ferric pyrophosphate citrate solution (triferic), 0.1 mg of iron
J1444	Injection, ferric pyrophosphate citrate powder, 0.1 mg of iron
J1445	Injection, ferric pyrophosphate citrate solution (triferic avnu), 0.1 mg of iron

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created per February SDC.	02.21.23	05.23
Per health plan request and SDC, added redirections from initial approval criteria to continued therapy.	08.15.23	
2Q 2024 annual review: no significant changes; added Venofer to Appendix B therapeutic alternatives table; references reviewed and updated.	01.12.23	05.24

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. 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.