

Injectafer® (ferric carboxymaltose injection) (Intravenous)

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I. Length of Authorization ¹

Coverage will be provided for 35 days, unless otherwise specified.

- Iron Deficiency in Patients with Heart Failure: Coverage will be provided for 12 weeks (for up to 2 doses) initially and may be renewed every 12 weeks (for 1 dose) up to a total of 3 maintenance doses.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Injectafer 100 mg iron/2 mL single-dose vial: 7 vials per 42 days
- Injectafer 750 mg iron/15 mL single-dose vial: 2 vials per 42 days
- Injectafer 1,000 mg iron/20 mL single-dose vial: 2 vial per 42 days

B. Max Units (per dose and over time) [HCPCS Unit]:

- Iron Deficiency in Patients with Heart Failure
 - Initial Dose: 2000 billable units per 42 days
 - Maintenance Dose: 500 billable units every 84 days
- All Other Indications: 1500 billable units per 35 days

III. Initial Approval Criteria ¹⁻¹³

Coverage is provided in the following conditions:

- Patient had an inadequate response, or has a contraindication or intolerance, to sodium ferric gluconate complex (Ferrlecit®) OR iron dextran (INFeD®) OR iron sucrose (Venofer®); **AND**
- Patient is at least 18 years of age, unless otherwise specified; **AND**
- Laboratory values must be obtained within 28 days prior to the anticipated date of administration; **AND**

- Other causes of anemia (e.g., vitamin B-12 deficiency, thalassemia, sideroblastic anemia, etc.) have been ruled out; **AND**
- Patient does not have a history of allergic reaction to any intravenous iron product; **AND**
- Other supplemental iron is to be discontinued prior to administration of ferric carboxymaltose; **AND**

Iron Deficiency Anemia in Non-Dialysis-Dependent Chronic Kidney Disease (NDD-CKD) †^{1,6,12}

- Patient must not be receiving dialysis; **AND**
- Patient has iron-deficiency anemia with a Hemoglobin (Hb) <11.5 g/dL; **AND**
 - Ferritin ≤100 ng/mL; **OR**
 - Ferritin ≤300 ng/mL when transferrin saturation (TSAT) ≤30%

Iron Deficiency Anemia in patients intolerant to or who have had unsatisfactory response to oral iron †¹⁻³

- Patient is at least 1 year of age; **AND**
- Patient had an intolerance or inadequate response to a minimum of 14 days of oral iron; **AND**
- Patient has iron-deficiency anemia with a Hemoglobin (Hb) <12 g/dL; **AND**
 - Ferritin ≤100 ng/mL; **OR**
 - Ferritin ≤300 ng/mL when transferrin saturation (TSAT) ≤30%

Cancer- and Chemotherapy-Induced Anemia †^{7,8,14,15}

- Used as a single agent; **AND**
 - Patient has absolute iron deficiency defined as ferritin < 30 ng/mL AND a TSAT < 20%; **OR**
 - Patient has functional iron deficiency defined as a ferritin > 500 - 800 ng/mL AND a TSAT < 50% with the goal of avoiding allogenic transfusion; **OR**
- Used in combination with erythropoiesis-stimulating agents (ESAs); **AND**
 - Patient has absolute iron deficiency defined as ferritin < 30 ng/mL AND a TSAT < 20% and failed to demonstrate an increase in Hb after 4 weeks of IV or oral iron therapy; **OR**
 - Patient has functional iron deficiency defined as ferritin 30 - 500 ng/mL AND a TSAT < 50% and is receiving myelosuppressive chemotherapy without curative intent

Iron Deficiency in Patients with Heart Failure †¹

- Patient has New York Heart Association class II/III disease; **AND**
- Used to improve exercise capacity; **AND**
- Patient has iron deficiency with hemoglobin < 15 g/dL; **AND**
 - Ferritin < 100 ng/mL; **OR**

- Ferritin is 100 to 300 ng/mL with TSAT <20%

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Ⓞ Orphan Drug

IV. Renewal Criteria ¹⁻¹³

Coverage may be renewed based on the following criteria:

Iron Deficiency in Patients with Heart Failure

- Patient has hemoglobin < 15 g/dL; **AND**
- Patient has serum ferritin <100 ng/mL OR serum ferritin 100-300 ng/mL with transferrin saturation <20%; **AND**
- Patient will receive maintenance doses at weeks 12, 24, and 36 (*Refer to dosing table below*)

****Note:** Patient may *ONLY* receive the maintenance doses if iron labs meet the aforementioned criteria. Patients not meeting this criteria will not be eligible for renewal.

All Other Indications

- Refer to initiation criteria.

V. Dosage/Administration ^{1,7}

| Indication | Dose |
|---|---|
| Iron Deficiency Anemia due to NDD-CKD or intolerance/inadequate response to oral iron | <p><u>Weight ≥ 50 kg:</u></p> <ul style="list-style-type: none"> • Administer two doses of 750 mg intravenously separated by at least 7 days for a total cumulative dose not to exceed 1500 mg of iron per course; OR • Administer one dose of 15 mg/kg body weight intravenously up to a maximum of 1,000 mg of iron per course <p><u>Weight < 50 kg:</u></p> <ul style="list-style-type: none"> • Administer two doses of 15 mg/kg body weight intravenously separated by at least 7 days for a total cumulative dose not to exceed 1500 mg of iron per course. <p>Treatment may be repeated if iron deficiency anemia reoccurs.</p> |
| Iron Deficiency with Heart Failure | <p>Initial Dosing</p> <p><u>Weight < 70 kg:</u></p> <ul style="list-style-type: none"> • Hb < 10 g/dL: Administer 1,000 mg intravenously on day 1 and 500 mg at week 6 • Hb 10 to 14 g/dL: Administer 1,000 mg intravenously on day 1 as a single dose (no dose at week 6) |

| | |
|---|--|
| | <ul style="list-style-type: none"> Hb >14 to <15 g/dL Administer 500 mg intravenously on day 1 as a single dose (no dose at week 6) <p><u>Weight ≥ 70 kg:</u></p> <ul style="list-style-type: none"> Hb <10 g/dL: Administer 1,000 mg intravenously on day 1 and 1,000 mg at week 6 Hb 10 to 14 g/dL: Administer 1,000 mg intravenously on day 1 and 500 mg at week 6 Hb > 14 to <15 g/dL: Administer 500 mg intravenously on day 1 as a single dose (no dose at week 6) <p>Maintenance Dosing</p> <ul style="list-style-type: none"> Administer 500 mg intravenously at 12, 24 and 36 weeks if serum ferritin <100 ng/mL or serum ferritin 100-300 ng/mL with transferrin saturation <20%. There are no data available to guide dosing beyond 36 weeks or with Hb ≥15 g/dL. |
| <p>Cancer/Chemotherapy Induced Anemia</p> | <p><u>Weight ≥ 50 kg:</u></p> <ul style="list-style-type: none"> Administer two doses of 750 mg intravenously separated by at least 7 days for a total cumulative dose not to exceed 1500 mg of iron per course <p><u>Weight < 50 kg:</u></p> <ul style="list-style-type: none"> Administer two doses of 15 mg/kg body weight intravenously separated by at least 7 days for a total cumulative dose not to exceed 1500 mg of iron per course. |

VI. Billing Code/Availability Information

HCPCS Code:

- J1439 - Injection, ferric carboxymaltose, 1 mg; 1 billable unit = 1 mg

NDC(s):

- Injectafer 100 mg iron/2 mL single-dose vial: 00517-0602-xx
- Injectafer 750 mg iron/15 mL single-dose vial: 00517-0650-xx
- Injectafer 1,000 mg iron/20 mL single-dose vial: 00517-0620-xx

VII. References

- Injectafer [package insert]. Shirley, NY; American Regent, Inc. May 2023. Accessed November 2023.

2. Onken JE, Bregman DB, Harrington RA, et al. A multicenter, randomized, active-controlled study to investigate the efficacy and safety of intravenous ferric carboxymaltose in patients with iron deficiency anemia. *Transfusion*. 2014 Feb;54(2):306-15.
3. Onken JE, Bregman DB, Harrington RA, et al. Ferric carboxymaltose in patients with iron-deficiency anemia and impaired renal function: the REPAIR-IDA trial. *Nephrol Dial Transplant*. 2014 Apr;29(4):833-42.
4. KDOQI; National Kidney Foundation. Clinical practice guidelines and clinical practice recommendations for anemia in chronic kidney disease in adults. *Am J Kidney Dis*. 2006 May;47(5 Suppl 3):S16-85.
5. Kidney Disease: Improving Global Outcomes (KDIGO) Anemia Work Group. KDIGO Clinical Practice Guideline for Anemia in Chronic Kidney Disease. *Kidney inter., Suppl*. 2012; 2: 279–335.
6. Ratcliffe LE, Thomas W, Glen J, et al. Diagnosis and Management of Iron Deficiency in CKD: A Summary of the NICE Guideline Recommendations and Their Rationale. *Am J Kidney Dis*. 2016 Apr;67(4):548-58.
7. Referenced with permission from the NCCN Drugs and Biologics Compendium (NCCN Compendium[®]) ferric carboxymaltose. National Comprehensive Cancer Network, 2023. The NCCN Compendium[®] is a derivative work of the NCCN Guidelines[®]. NATIONAL COMPREHENSIVE CANCER NETWORK[®], NCCN[®], and NCCN GUIDELINES[®] are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed November 2023.
8. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines[®]) Hematopoietic Growth Factors Version 1.2024. National Comprehensive Cancer Network, 2023. The NCCN Compendium[®] is a derivative work of the NCCN Guidelines[®]. NATIONAL COMPREHENSIVE CANCER NETWORK[®], NCCN[®], and NCCN GUIDELINES[®] are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed November 2023.
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11. Steinmetz T, Tschekne B, Harlin O, et al. Clinical experience with ferric carboxymaltose in the treatment of cancer- and chemotherapy-associated anaemia. *Ann Oncol*. 2013;24(2):475-482.
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13. Ponikowski P, van Veldhuisen DJ, Comin-Colet J, et al; CONFIRM-HF Investigators. 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.

14. Makharadze T, Boccia R, Krupa A, et al. Efficacy and safety of ferric carboxymaltose infusion in reducing anemia in patients receiving chemotherapy for nonmyeloid malignancies: A randomized, placebo-controlled study (IRON-CLAD). Am J Hematol 2021;96:1639-1646.
15. Toledano A, Luporsi E, Morere JF, et al. Clinical use of ferric carboxymaltose in patients with solid tumours or haematological malignancies in France. Support Care Cancer 2016;24:67-75.

Appendix 1 – Covered Diagnosis Codes

| ICD-10 | ICD-10 Description |
|--------|--|
| D50.0 | Iron deficiency anemia secondary to blood loss (chronic) |
| D50.1 | Sideropenic dysphagia |
| D50.8 | Other iron deficiency anemias |
| D50.9 | Iron deficiency anemia, unspecified |
| D63.0 | Anemia in neoplastic disease |
| D63.1 | Anemia in chronic kidney disease |
| D63.8 | Anemia in other chronic disease classified elsewhere |
| D64.81 | Anemia due to antineoplastic chemotherapy |
| Z51.11 | Encounter for antineoplastic chemotherapy |
| Z51.89 | Encounter for other specified aftercare |

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: <http://www.cms.gov/medicare-coverage-database/search.aspx>. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

| Medicare Part B Administrative Contractor (MAC) Jurisdictions | | |
|---|--|---|
| Jurisdiction | Applicable State/US Territory | Contractor |
| E (1) | CA, HI, NV, AS, GU, CNMI | Noridian Healthcare Solutions, LLC |
| F (2 & 3) | AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ | Noridian Healthcare Solutions, LLC |
| 5 | KS, NE, IA, MO | Wisconsin Physicians Service Insurance Corp (WPS) |
| 6 | MN, WI, IL | National Government Services, Inc. (NGS) |
| H (4 & 7) | LA, AR, MS, TX, OK, CO, NM | Novitas Solutions, Inc. |

| Medicare Part B Administrative Contractor (MAC) Jurisdictions | | |
|---|---|---|
| Jurisdiction | Applicable State/US Territory | Contractor |
| 8 | MI, IN | Wisconsin Physicians Service Insurance Corp (WPS) |
| N (9) | FL, PR, VI | First Coast Service Options, Inc. |
| J (10) | TN, GA, AL | Palmetto Government Benefit Administrators, LLC |
| M (11) | NC, SC, WV, VA (excluding below) | Palmetto GBA, LLC |
| L (12) | DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA) | Novitas Solutions, Inc. |
| K (13 & 14) | NY, CT, MA, RI, VT, ME, NH | National Government Services, Inc. (NGS) |
| 15 | KY, OH | CGS Administrators, LLC |