

**POLICY:** Iron Replacement – Ferrlecit® (sodium ferric gluconate complex in sucrose injection, for intravenous use – sanofi-aventis)

**DATE REVIEWED:** 12/18/2019; selected revision 03/04/2020

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## OVERVIEW

Ferrlecit is an iron replacement product indicated for treatment of iron deficiency anemia in adults and pediatric patients  $\geq 6$  years of age with chronic kidney disease (CKD) receiving hemodialysis who are receiving supplemental epoetin therapy.<sup>1</sup> Ferrlecit is administered by intravenous (IV) infusion or slow injection and treatment may be repeated if iron deficiency remains persistent or recurring. The recommended dosage of Ferrlecit for the repletion treatment of iron deficiency in hemodialysis patients is 10 mL of Ferrlecit (125 mg of elemental iron). For repletion treatment most adult patients may require a cumulative dose of 1000 mg of elemental iron administered over 8 dialysis sessions. The recommended pediatric dosage in hemodialysis patients is 0.12 mL/kg Ferrlecit (1.5 mg/kg of elemental iron) administered by intravenous infusion per dialysis session. The maximum pediatric dosage should not exceed 125 mg per dose.

## Disease Overview

Iron deficiency anemia is a very broad diagnosis and can have many different etiologies; underlying causes should be corrected when appropriate. Anemia is generally characterized by a decrease in hemoglobin (Hb) or in the volume of red blood cells, which decrease the oxygen-carrying capacity in the blood.<sup>2</sup> Anemia is defined by the World Health Organization as Hb  $< 13.0$  g/dL in men,  $< 12.0$  g/dL in women, and  $< 11$  g/dL during pregnancy.<sup>2,3</sup> Acute-onset anemia can present with tachycardia, lightheadedness, and shortness of breath.<sup>2</sup> Chronic anemia can manifest as weakness, fatigue, headache, dizziness, and pallor. Worldwide, iron deficiency is the most common nutritional deficiency. Anemia is prevalent in patients with CKD and the frequency and severity of anemia may increase with declining renal function. The severity and causes are variable and it can be a sign of other illnesses. Iron deficiency anemia is characterized by decreased levels of ferritin and serum iron, as well as decreased transferrin saturation (TSAT); decreases in Hb and hematocrit may follow.

## Guidelines

The KDIGO guidelines for anemia in CKD (2012) make various recommendations regarding iron therapy.<sup>4</sup> For adults with CKD and anemia not on iron or erythropoietin stimulating agent (ESA) therapy, a trial of IV iron (or in non-dialysis patients with CKD, alternatively, a 1 to 3 month trial of oral iron therapy) is recommended if an increase in Hb concentration without starting ESA treatment is desired and TSAT is  $\leq 30\%$  and ferritin is  $\leq 500$  ng/mL. For adults with CKD on ESA therapy who are not receiving iron supplementation, a trial of IV iron (or in non-dialysis CKD patients, alternatively, a 1 to 3 month trial of oral iron therapy) is recommended if an increase in Hb concentration or a decrease in ESA dose is desired and TSAT is  $\leq 30\%$  and ferritin is  $\leq 500$  ng/mL. For all pediatric patients with CKD with anemia not on iron or ESA therapy, oral iron (or IV iron in patients receiving hemodialysis) is recommended when TSAT is  $\leq 20\%$  and ferritin is  $\leq 100$  ng/mL. For all pediatric patients with CKD who are receiving ESA therapy but not receiving iron supplementation, it is recommended to administer oral iron (or IV iron for patients receiving hemodialysis) to maintain TSAT  $> 20\%$  and ferritin  $> 100$  ng/dL.

## Other Uses with Supportive Evidence

A 2017 focused update of the 2013 American College of Cardiology Foundation/American Heart Association guideline for the management of heart failure. It states that patients with New York Heart Association class II or III heart failure, absolute iron deficiency (ferritin  $< 100$  ng/mL) or functional iron

deficiency (ferritin 100 to 300 mg/mL if TSAT is < 20%), and with or without anemia, IV iron replacement may be reasonable to improve functional status and quality of life.<sup>5</sup> Benefits noted with IV iron therapies included improvement in functional capacity and improvements in the six-minute walk test.

The National Comprehensive Cancer Network guidelines on Hematopoietic Growth Factors (version 1.2020 – November 15, 2019) discuss the management of cancer- and chemotherapy-induced anemia.<sup>6</sup> IV iron therapy is considered an option for patients with absolute iron deficiency (ferritin < 30 ng/mL and TSAT < 20%), functional iron deficiency (ferritin = 30 to 500 ng/mL and TSAT < 50%), and possible functional iron deficiency (ferritin = 501 to 800 ng/mL and TSAT < 50%).

### **POLICY STATEMENT**

Prior authorization is recommended for medical benefit coverage of Ferrlecit. Approval is recommended for those who meet the Criteria and Dosing for the listed indication(s). For patients with chronic kidney disease who are on dialysis, prior authorization is not required for medical benefit coverage. All approvals are provided for the duration noted below. Requests for doses outside the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). Because of the specialized skills required for evaluation and diagnosis of patients treated with Ferrlecit as well as the monitoring required for adverse events and long-term efficacy, approval requires Ferrlecit to be prescribed by or in consultation with a physician who specializes in the condition being treated in some circumstances.

### **RECOMMENDED AUTHORIZATION CRITERIA**

#### **FDA-Approved Indications**

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**1. Iron Deficiency Anemia in Patients with Chronic Kidney Disease who are on Dialysis.** Approve for 3 years.

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**2. Iron Deficiency Anemia in Patients with Chronic Kidney Disease who are not on Dialysis.** Approve for 1 year if the product meets the following criteria (A and B):

- A) The patient is  $\geq 6$  years of age; AND
- B) Ferrlecit is prescribed by, or in consultation with, a nephrologist or hematologist.

**Dosing.** Approve up to a maximum cumulative total dose of 1000 mg given intravenously per 30 days.

#### **Other Uses with Supportive Evidence**

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**3. Iron Deficiency Anemia, Other.** Approve for 1 year if the patient meets the following (A and B):

- A) The patient is  $\geq 6$  years of age; AND
- B) The patient meets one of the following (i, ii, iii, or iv):
  - i. The patient meets both of the following (a and b):
    - a) The patient has tried oral iron supplementation; AND
    - b) According to the prescriber, oral iron supplementation was ineffective or intolerable; OR
  - ii. The patient has a condition which, per the prescriber, will interfere with oral iron absorption (e.g., inflammatory bowel disease, Crohn's disease); OR

- iii. The patient is currently receiving an erythroid stimulating agent; OR  
Note: Examples of erythroid stimulating agents include an epoetin alfa product, a darbepoetin alfa product, or a methoxy polyethylene glycol-epoetin beta product.
- iv. The medication is being requested for cancer- or chemotherapy-related anemia.

**Dosing.** Approve up to a maximum cumulative total dose of 1000 mg given intravenously per 30 days.

4. **Iron Deficiency Associated with Heart Failure.** Approve for 1 year if the product meets the following criteria (A and B):

- A) The patient is  $\geq 6$  years of age; AND
- B) Ferrlecit is being prescribed by, or in consultation with, a cardiologist or hematologist.

**Dosing.** Approve up to a maximum cumulative total dose of 1000 mg given intravenously per 30 days.

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### CONDITIONS NOT RECOMMENDED FOR APPROVAL

Ferrlecit has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

- 1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

### REFERENCES

- 1. Ferrlecit® [prescribing information]. Bridgewater, NJ: sanofi-aventis; September 2019.
- 2. Cook K, Ineck BA, Lyons WL. Anemias. In: Dipro JT, Talbert RL, Yee GC, et al, (Eds). Pharmacotherapy – A Pathophysiologic Approach. 8<sup>th</sup> Ed, New York, NY: McGraw-Hill Companies, Inc. 2011:1717-1740.
- 3. Camaschella C. Iron deficiency. *Blood*. 2019;133(1):30-39.
- 4. Kidney Disease: Improving Global Outcomes (KDIGO) Anemia Work Group. KDIGO Clinical Practice Guideline for Anemia in Chronic Kidney Disease. *Kidney Int*. 2012;2(Suppl):279-335.
- 5. Yancy CW, Jessup M, Bozkurt B, et al. 2017 ACC/AHA/HFSA focused update of the 2013 ACCF/AHA guideline for the management of heart failure. *J Am Coll Cardiol*. 2017;70(6):776-803.
- 6. The NCCN® Hematopoietic Growth Factors Guidelines in Oncology (Version 2.2020 – January 27, 2020). 2020 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org/clinical.asp>. Accessed on February 4, 2020.

### HISTORY

Type of Revision	Summary of Changes	Date Reviewed
New policy	--	12/18/2019
Selected Revision	<b>Iron Deficiency Anemia in Chronic Kidney Disease</b> was separated into two conditions, <b>Iron Deficiency Anemia in Patients with Chronic Kidney Disease who are on Dialysis</b> and <b>Iron Deficiency Anemia in Patients with Chronic Kidney Disease who are not on Dialysis</b> . The indication for <b>Iron Deficiency Anemia in Patients with Chronic Kidney Disease who are on Dialysis</b> will not be targeted in this policy and all requests are to approve for 3 years.	03/04/2020