MEDICATION COVERAGE POLICY

PHARMACY AND THERAPEUTICS ADVISORY COMMITTEE

POLICY:	ESA/Anemia of Chronic Disease	**P&T DATE:**	01/12/2024
CLASS:	Renal Disease/Genitourinary Disorders	**REVIEW HISTORY:** (MONTH/YEAR)	12/22,12/21, 2/21, 2/20, 2/19, 9/17, 12/16, 9/15, 9/11, 2/11
LOB:	MCL		

This policy has been developed through review of medical literature, consideration of medical necessity, generally accepted medical practice standards, and approved by the HPSJ Pharmacy and Therapeutic Advisory Committee.

Effective 1/1/2022, the Pharmacy Benefit is regulated by Medi-Cal Rx. Please visit https://medi-calrx.dhcs.ca.gov/home/ for portal access, formulary details, pharmacy network information, and updates to the pharmacy benefit.

All medical claims require that an NDC is also submitted with the claim. If a physician administered medication has a specific assigned CPT code, that code must be billed with the correlating NDC. If there is not a specific CPT code available for a physician administered medication, the use of unclassified CPT codes is appropriate when billed with the correlating NDC.

OVERVIEW

The purpose of this coverage policy is to review the available agents (Table 1) and distinguish where the medications may be billed to. For agents listed for coverage under the medical benefit, this coverage is specific to outpatient coverage only (excludes emergency room and inpatient coverage).

Table 1: Available Agents (*Current as of 1/2024****):***

CPT code	Generic Name (Brand Name)	Available Strengths	Pharmacy Benefit	Outpatient Medical Benefit (Restrictions)
Iron				
--	Carbonyl Iron (Icar Pediatric, Feosol Caplets)	15 mg chewable Tablets, 45mg Tablets, 15mg/1.25mL Suspension	Yes	No
J1750	Iron Dextran Complex (Infed)	50 mg/mL (2 mL) injection, solution	Yes	Yes
J2916	Ferric Gluconate (Ferrlecit)	62.5 mg/5ml Vial	Yes	Yes
J1756	Iron Sucrose (Venofer)	200 mg/10 mL, 100mg/5mL, 50mg/2.5mL IV Solution	Yes	Yes (PA)
Q0139 **Q0138**	Ferumoxytol (Feraheme)	510 mg/17ml Vial	Yes	Yes (PA)
J1439	Ferric Carboxymaltose (Injectafer)	750 mg/15ml Vial	Yes	Yes (PA)
--	Ferric Citrate (Auryxia)	210 mg Tablet	Yes	No
--	Ferrous Fumarate (Hemocyte)	324 mg Tablet (106 mg elemental iron)	Yes	No
--	Ferrous Gluconate (Fergon)	324 mg Tablet (38 mg elemental iron)	Yes	No
--	Ferrous Gluconate, preservative free (Ferate)	324 mg Tablet (37.5 mg elemental iron)	Yes	No
--	Ferrous Sulfate (Ferosul, Fer-In-Sol)	325mg IR Tablet, 324mg DR Tablet, 325mg ER Capsule, 15mg/mL Drops, 220mg/5mL Solution,	Yes	No

		300mg/5mL Liquid,		
--	Polysaccharide-iron Complex (Ferrex-150)	150 mg	Yes	No
Erythropoietin Stimulating Agents (ESA)				
Q5105 (for ESRD) **Q5106**	Epoetin Alfa (Retacrit)	2,000 Unit/mL Injection Solution 3,000 Unit/mL Injection Solution 4,000 Unit/mL Injection Solution 10,000 Unit/mL Injection Solution 40,000 Unit/mL Injection Solution	Yes	Yes (PA)
J0885 **Q4081 (for ESRD)**	Epoetin Alfa (Epogen, Procrit)	2,000 Unit/mL Injection Solution 3,000 Unit/mL Injection Solution 4,000 Unit/mL Injection Solution 10,000 Unit/mL Injection Solution 20,000 Unit/mL Injection Solution 40,000 Unit/mL Injection Solution	Yes	Yes (PA)
J0881 **J0882 (for ESRD)**	Darbepoetin Alfa (Aranesp)	25 mcg/mL Injection Solution 40 mcg/mL Injection Solution 60 mcg/mL Injection Solution 100 mcg/mL Injection Solution 200 mcg/mL Injection Solution 300 mcg/mL Injection Solution 10 mcg/0.4 mL Prefilled Syringe 25 mcg/0.42 mL Prefilled Syringe 40 mcg/0.4 mL Prefilled Syringe 60 mcg/0.3 mL Prefilled Syringe 100 mcg/0.5 mL Prefilled Syringe 150 mcg/0.3 mL Prefilled Syringe 200 mcg/0.4 mL Prefilled Syringe 300 mcg/0.6 mL Prefilled Syringe 500 mcg/mL Prefilled Syringe	Yes	Yes (PA)
J0887 (for ESRD) **J0888**	Methoxy Polyethylene Glycol-Epoetin Beta (Mircera)	30 mcg/0.3 mL Prefilled Syringe 50 mcg/0.3 mL Prefilled Syringe 75 mcg/0.3 mL Prefilled Syringe 100 mcg/0.3 mL Prefilled Syringe 150 mcg/0.3 mL Prefilled Syringe 200 mcg/0.3 mL Prefilled Syringe	Yes	Yes (PA)

EVALUATION CRITERIA FOR APPROVAL/EXCEPTION CONSIDERATION

Below are the coverage criteria and required information for agents with medical benefit restrictions. This coverage criteria has been reviewed and approved by the HPSJ Pharmacy & Therapeutics (P&T) Advisory Committee. For agents that do not have established prior authorization criteria, HPSJ will make the determination based on Medical Necessity criteria as described in HPSJ Medical Review Guidelines (UM06).

Iron Supplements

Iron Dextran (Infed)

- ❒ **Coverage Criteria:** None
- ❒ **Limits:** None
- ❒ **Required Information for Approval:** N/A

Ferric Gluconate (Ferrlecit)

- ❒ **Coverage Criteria:** None
- ❒ **Limits:** None
- ❒ **Required Information for Approval:** N/A

Iron Sucrose (Venofer)

- ❒ **Coverage Criteria:** Reserved for patients with one or more of the following:
  a) Absolute iron deficiency anemia with a ferritin <30µg/L or TSAT <20% with treatment failure or inability to tolerate oral iron.
  b) Chronic kidney disease with or without dialysis with ferritin < 500µg/L and TSAT <30% with treatment failure or inability to tolerate oral iron for non-dialysis patients.
  c) Chemotherapy-induced anemia with ferritin 30-500µg/L **or** TSAT <50% in patients receiving ESAs. Ferritin must not exceed 800µg/L, and TSAT must not be ≥50%.
- ❒ **Limits:** Limited to 1,200 mg per treatment cycle.
- ❒ **Required Information for Approval:** Updated ferritin **and/or** TSAT levels with documented history of treatment failure or inability to tolerate oral iron.
- ❒ **Other Notes:** None

Ferumoxytol (Feraheme)

- ❒ **Coverage Criteria:** Reserved for patients with one or more of the following:
  a) Absolute iron deficiency anemia with a ferritin <30µg/L or TSAT <20% with treatment failure or inability to tolerate oral iron.
  b) Chronic kidney disease with or without dialysis with ferritin < 500µg/L and TSAT <30% with treatment failure or inability to tolerate oral iron for non-dialysis patients.
  c) Chemotherapy-induced anemia with ferritin 30-500µg/L **or** TSAT <50% in patients receiving ESAs. Ferritin must not exceed 800µg/L, and TSAT must not be ≥50%.
- ❒ **Limits:** None
- ❒ **Required Information for Approval:** Updated ferritin and/or TSAT levels with documented history of treatment failure or inability to tolerate oral iron.

Ferric carboxymaltose (Injectafer)

- ❒ **Coverage Criteria:** Reserved for patients with one or more of the following **AND has documented history of treatment failure or inability to tolerate Venofer or Feraheme**:
  d) Absolute iron deficiency anemia with a ferritin <30µg/L or TSAT <20% with treatment failure or inability to tolerate oral iron.
  e) Chronic kidney disease with or without dialysis with ferritin < 500µg/L and TSAT <30% with treatment failure or inability to tolerate oral iron for non-dialysis patients.
  f) Chemotherapy-induced anemia with ferritin 30-500µg/L **or** TSAT <50% in patients receiving ESAs. Ferritin must not exceed 800µg/L, and TSAT must not be ≥50%.
- ❒ **Limits:** None
- ❒ **Required Information for Approval:** Updated ferritin and/or TSAT levels with documented history of treatment failure or inability to tolerate oral iron.

Erythropoietin Stimulating Agents (ESA)

Epoetin Alfa (Retacrit, Epogen, Procrit)

- ❒ **Coverage Criteria:**
  - **Retacrit, Epogen, or Procrit** are reserved for patients who have Hemoglobin (Hgb) < 10 g/dl, with TSAT > 20% **or** serum ferritin > 100 ng/ml at initiation. Hgb should be checked monthly and is not to exceed 11 g/dl. Authorization is for **12** months at a time. For renewal, Hgb must be below 11 g/dL.
- ❒ **Limits:** Restricted to Diplomat Specialty Pharmacy. When initiating therapy for anemia due to CKD, cumulative weekly dosing does not exceed the target range of 50 to 100 units/kg 3 times a week (300 units/kg weekly).
- ❒ **Required Information for Approval:** Submit chart notes including the patient's most recent iron studies and CBC.
- ❒ **Additional Notes:**
  - Epoetin is approved for **12** months at a time.
  - Submission of Hgb levels with the prior authorization renewal request is required and must not exceed 11g/dL.

Darbepoetin Alfa (Aranesp)

- ❒ **Coverage Criteria:**
  - Aranesp is reserved for patients who have
    - Hemoglobin (Hgb) < 10 g/dl, with TSAT > 20% **or** serum ferritin > 100 ng/ml at initiation
  - Hgb should be checked monthly and is not to exceed 11 g/dl.
  - Authorization is for **12** months at a time. For renewal, Hgb must be below 11 g/dL.
- ❒ **Limits:** When initiating therapy for anemia due to CKD, cumulative weekly dosing does not exceed the target range of 0.45 mcg/kg once weekly or 0.75 mcg/kg once every 2 weeks.
- ❒ **Required Information for Approval:** Submit chart notes including the patient's most recent iron studies and CBC.
- ❒ **Additional Notes:**
  - is approved for **12** months at a time.
  - Submission of Hgb levels with the prior authorization renewal request is required and must not exceed 11g/dL.

Epoetin Beta (Mircera)

- ❒ **Coverage Criteria:**
  - Mircera is reserved for patients who have
    - Hemoglobin (Hgb) < 10 g/dl, with TSAT > 20% **or** serum ferritin > 100 ng/ml at initiation
  - Hgb should be checked monthly and is not to exceed 11 g/dl.
  - Authorization is for **12** months at a time. For renewal, Hgb must be below 11 g/dL.
- ❒ **Limits:** When initiating therapy for anemia due to CKD, cumulative weekly dosing does not exceed the target range 0.6 mcg/kg once every 2 weeks.
- ❒ **Required Information for Approval:** Submit chart notes including the patient's most recent iron studies and CBC.
- ❒ **Additional Notes:**
  - is approved for **12** months at a time.
  - Submission of Hgb levels with the prior authorization renewal request is required and must not exceed 11g/dL.

⌗ CLINICAL JUSTIFICATION

Studies have shown that patients who used Epoetin Alfa to target normal levels of Hgb had poor cardiovascular outcomes. These trials showed increases in mortality, nonfatal MI, and hospitalization for CHF. ESA therapy should target a Hemoglobin of less than 11 g/dL. In essence, patients should be treated only to avoid blood transfusion. Iron supplementation is required for most patients with CKD, especially those taking ESAs. Various dosage forms of ferrous sulfate are available on formulary without restriction.

Triage:

1. Duration of Membership
2. Appropriate Diagnosis
3. Current Hemoglobin and Iron studies (TSAT, Ferritin, MCV, Serum Iron)
4. Prescribing Physician Specialty

Updated guidelines and literature will be used for the creation of criteria of iron sucrose and ferumoxytol for patients with absolute iron deficiency anemia, chronic kidney disease (CKD), and chemotherapy-induced anemia in patients receiving erythropoietin stimulating agents (ESAs).

Absolute iron deficiency anemia is defined as low iron stores for which ferritin is the most reliable initial test for diagnosis. A threshold of ferritin ≤30 µg/L achieves a high sensitivity (92%) while maintaining a high 98%

specificity for the diagnosis and is thus commonly used. In cases in which ferritin is increased with concomitant inflammatory conditions a transferrin saturation (TSAT) <20% can be used for diagnosis.[16]

The 2012 KDIGO Clinical Practice Guideline for Anemia in Chronic Kidney Disease suggest iron administration in anemic CKD patients with TSAT <30% and serum ferritin ≤500 ng/ml if an increase in hemoglobin level is desired, particularly if intended to avoid transfusions and reduce anemia-related symptoms, and/or reduction in ESA dose. IV iron is recommended for dialysis patients while oral iron is an alternative in non-dialysis patients.[3]

The 2020 NCCN Guidelines for Hematopoietic Growth Factors state that iron supplementation should be considered for absolute iron deficiency with ferritin <30 µg/L and TSAT <20% or functional iron deficiency anemia in patients receiving ESAs with ferritin 30-500 µg/L and TSAT <50%. For patients with functional iron deficiency on ESAs, IV iron is recommended over oral iron as there has shown to be superior efficacy with IV iron in this population.

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22. Retacrit (epoetin alfa-epbx) [prescribing information]. Lake Forest, IL: Hospira, Inc; September 2020.

⌗ REVIEW & EDIT HISTORY

Document Changes	Reference	Date	P&T Chairman
Creation of Policy	Parenteral Iron Therapeutic Class Review 2-15-11.docx	2/2011	Allen Shek, PharmD BCPS
Update to Policy	ESA Criteria Review 9-20-11.docx	9/2011	Allen Shek, PharmD BCPS
Update to Policy	HPSJ Coverage Policy - Renal - Anemia 2015-09.docx	9/2015	Jonathan Szkotak, PharmD, BCPCS
Update to Policy	HPSJ Coverage Policy - Renal - Anemia 2016-12.docx	12/2016	Johnathan Yeh, PharmD
Update to Policy	HPSJ Coverage Policy - Renal - Anemia 2017-09.docx	9/2017	Johnathan Yeh, PharmD
Update to Policy	HPSJ Coverage Policy - Renal - Anemia 2019-02.docx	2/2019	Matthew Garrett, PharmD
Update to Policy	HPSJ Coverage Policy - Renal - Anemia.docx	2/2020	Matthew Garrett, PharmD
Update to Policy	HPSJ Coverage Policy - Renal - Anemia 2021-02.docx	2/2021	Matthew Garrett, PharmD
Update to Policy	Anemia	12/2021	Matthew Garrett, PharmD
Update to Policy	Anemia	12/2022	Matthew Garrett, PharmD
Review of Policy	Anemia	1/2024	Matthew Garrett, PharmD

Note: All changes are approved by the HPSJ P&T Committee before incorporation into the utilization policy