INDIAN HEALTH SERVICE
National Pharmacy and Therapeutics Committee
Formulary Brief: Anemia of Chronic Kidney Disease
-February 2026-

Background:

The Indian Health Service (IHS) National Pharmacy and Therapeutics Committee (NPTC) provided a pharmacotherapeutic review of agents related to the management of anemia with chronic kidney disease (CKD) in adult patients not on dialysis. Medications listed on the National Core Formulary (NCF) relevant to this condition include oral iron (any formulation). Following clinical review and analysis, the NPTC voted to make **no modifications** to the NCF.

Discussion:

Incidence, Mortality, and Economic Burden

According to Burrows et al., the IHS has higher rates of angiotensin-converting enzyme inhibitor (ACEi) and angiotensin receptor blocker (ARB) use compared to United States (U.S.) adults with diabetes (76% vs 56%). They report the incidence of diabetes-related end-stage kidney disease (ESKD) among American Indian/Alaska Native (AI/AN) people declined by 53% from 2000–2016.[1] Despite this decline, mortality rates from kidney disease remain elevated in AI/AN people: the IHS Disparities Fact Sheet indicates that in 2009–2011, the age-adjusted mortality rates per 100,000 individuals for kidney disease in AI/AN people were 50% higher than the U.S. all-races rate.[2]

Wittbrodt et al. reported that among patients with CKD, the economic burden and median total costs were substantially higher in those with anemia vs. those without anemia ($49,012 vs $31,667).[3] Iron (oral, intravenous [IV]) and erythropoiesis-stimulating agents (ESAs) remain mainstays to treat anemia of CKD. In 2022, ESA use among patients with ESKD in the AI/AN population was lower (13.4% compared with the U.S. all-races rate of 15.8%).[4]

IV Iron vs. Oral Iron

Initiating therapy with oral iron for anemia of CKD remains a reasonable and cost-effective strategy. Tolerability remains a major consideration when prescribing oral iron. The Kidney Disease: Improving Global Outcomes (KDIGO) guideline on anemia published in 2026 recommends switching from oral to IV iron if there is an insufficient effect resulting from an optimal oral regimen after 1 to 3 months.[5]

In the trial FIND-CKD (56 weeks), IV ferric carboxymaltose was compared with oral ferrous sulfate. The primary outcome was the time to initiation of other anemia management (ESAs, transfusions, or alternative iron) or a hemoglobin (Hb) trigger (<10 g/dL twice consecutively during weeks 8–52). IV ferric carboxymaltose reduced the risk over time of reaching the primary outcome vs. oral iron (hazard ratio 0.65, 95% CI: 0.44-0.95; p=0.026).[6] Although IV iron provides a fast repletion option, consider avoiding this route during active infections. Since several one- and two-dose full repletion IV iron options exist now, selection among IV iron products may be guided by acquisition cost and dose-completion logistics. During the NPTC review, studies largely agreed with the KDIGO recommendations that, in patients with CKD receiving iron (oral or IV), the choice of formulation and dosing schedule should be guided by safety, efficacy, tolerability, individual patient preference and cost.[5]

ESAs

A Cochrane systematic review and network meta-analysis of randomized controlled trials by Chung et al. showed that all ESAs tended to prevent blood transfusions and were also associated with an increased risk of hypertension.[7] Furthermore, a second Cochrane systematic review by Saglimbene et al. compared methoxy polyethylene glycol-epoetin beta against all other ESAs and placebo. The authors found no significant differences in mortality, major cardiovascular events, hospital admissions, vascular access thrombosis, cancer, quality of life, adverse effects including hypertension, hyperkalemia, seizures, and injection reactions.[8] These trials support KDIGO's statement that "in people with anemia and CKD treated with ESAs, administer ESAs with the lowest dose possible that achieves and maintains treatment goals."[5] ESA initiation and titration require frequent Hb monitoring and blood pressure management; this may be challenging in some service units.

Hypoxia Inducible Factor-Prolyl Hydroxylase Inhibitors (HIF-PHIs)

HIF-PHIs are a new class of oral medications and serve as alternatives to ESAs in patients who have been on dialysis for ≥3 months. Vadadustat is the only option currently marketed in the U.S and its use in non-dialysis patients is off-label.[9] Guidance in the 2026 KDIGO guidelines states that "In people with CKD, anemia, and ESA hypo responsiveness, if there is a desire to raise Hb to avoid transfusion or improve symptoms attributable to anemia, a trial course of HIF-PHI may be considered after discussion of potential risks and benefits."[5] At this time, HIF-PHIs are not recommended for routine non-dialysis CKD use in the IHS, given U.S. indication limitations and monitoring considerations.

Findings:

Anemia of non-dialysis CKD is often an undertreated condition, especially in the AI/AN population. Although ESAs offer no mortality benefit, treatment with ESAs may reduce blood transfusions and improve patients' quality of life. Preventing blood transfusions is an important goal, as it reduces the risk of allosensitization and subsequent rejection of kidney transplant later on.[5]

The 2026 KDIGO anemia guidelines note that hypersensitivity reactions to IV iron are rare and recommend that the first dose of IV iron be administered only in a setting with the capability to manage acute hypersensitivity and hypotensive reactions.[5] ESAs also require a certain level of expertise when administering and require frequent dosing adjustments. Because these requirements may not be consistently achievable across all IHS service units, no additions to the NCF were made. The committee did suggest that local service units consider, where feasible, the addition of an ESA and IV iron to local formularies.

National Core Formulary	No change (oral iron: any oral formulation)
Local Formularies	Encourage ESA(s) and IV iron where feasible
Feasibility	Requires education, infusion capability, reaction management resources, and lab monitoring protocols

Additionally, ferrous sulfate and ferrous gluconate remain the most common oral iron products used by IHS facilities. Programs can continue to use any oral iron when necessary to treat CKD-related anemia. Programs should be aware of newer, more expensive oral iron supplements as they become available and to use them judiciously.

If you have any questions regarding this document, please contact the NPTC at IHSNPTC1@ihs.gov. For more information about the NPTC, please visit the NPTC website.

References:

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