# Management of Iron Deficiency Anemia in Chronic Kidney Disease

Iron Corner
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## SUMMARY

- Anemia is common in chronic kidney disease (CKD) and may be managed with iron alone or in conjunction with erythropoietic stimulating agents (ESA).
- Left untreated, anemia has adverse effects on cardiac function, quality of life (QOL), CKD progression and survival.
- Intravenous iron remains a mainstay of anemia management in patients with CKD and end-stage renal disease (ESRD).


## How Common Is Iron Deficiency in CKD?

- CKD is a progressive disease that gradually impairs kidney function, usually over a period of years. According to the National Kidney Foundation (NKF), approximately 8 million people in the US are living with moderate (stage 3) or severe (stage 4) CKD and are not yet receiving dialysis.[1,3]
- CKD often progresses to ESRD, where the kidneys fail and renal replacement therapy such as dialysis or transplantation is required to sustain life.
- The primary goal of treatment for CKD is to slow the progression of the disease, mainly by controlling the underlying common causes: hypertension and/or diabetes.
- Patients with CKD suffer from a myriad of complications, which may also affect CKD progression and can include malnutrition, bone disease and anemia, usually accompanied by iron deficiency.

## What Causes Iron Deficiency (ID) in CKD?

- ID and anemia, often multifactorial in its etiology, are significant complications of CKD and ESRD, developing early in the course of the disease and progressing with loss of renal function.[2]
- Published data indicate that approximately 44% of patients with CKD stage 3 or 4 are anemic (defined as Hgb <13.5 g/dL for men and Hgb <12.0 g/dL for women), and the prevalence of anemia increases to 75% in patients reaching CKD stage 5 (ESRD).[1]
- The cause of this anemia is multi-factorial and includes the inability of the failing kidney to produce enough erythropoietin to stimulate adequate hematopoiesis, iron deficiency, and shortened red blood cell survival.
- ID is a common and often predominant cause of anemia in CKD patients.
- ID and iron deficiency anemia (IDA) can be due to both poor nutrition and blood loss and can be exacerbated by use of ESAs as ESA therapy depletes iron stores as iron needs are increased to produce iron-containing red blood cells (RBCs).

## Who Should Be Screened?

- All patients with CKD should be screened for anemia that includes iron studies.
- Although the anemia may be solely related to CKD, other causes should be excluded including occult GI bleeding and nutritional deficiencies such as B12 and folate.
- Iron status testing includes serum iron, total iron-binding capacity (TIBC), percent transferrin saturation (TSAT), and serum ferritin.

## Why Should Screening and Treatment Be Considered?

- Left untreated, anemia can have adverse effects on cardiac function, CKD progression, and survival.[4-7]
- Anemia has also been shown to be an independent predictor and risk multiplier for increased mortality in CKD patients who have not progressed to ESRD.
- Patients diagnosed with CKD and anemia have a risk of death that is equivalent to that in patients diagnosed with both diabetes and congestive heart failure combined.[5-8]
- Treatment of IDA in CKD stages 1 through 4 may be critical to reducing associated cardiovascular morbidity and mortality since anemia-associated left ventricular hypertrophy may be irreversible if therapy is delayed until the beginning of dialysis.[9]

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## What Iron Treatment Is Recommended?

- The treatment of anemia of CKD includes transfusion support, ESA and iron therapy. Evidence suggests that aggressive treatment of iron deficiency anemia earlier in the progression of CKD can improve quality of life as well as disease outcome and may possibly slow the progression to complete renal failure.[10-13]
- IV iron should be considered in anemic CKD patients who have a TSAT ≤20 percent and/or a serum ferritin concentration ≤100 ng/mL as these patients are likely to have decreased iron stores.
- Patients with a TSAT between 20% and 30% and a ferritin level between 100 and 500 ng/mL may also benefit from iron therapy if the hemoglobin is low enough to warrant an increase or to potentially avoid the use of an ESA.
- Individuals with a TSAT >30 percent would not be expected to benefit.
- Routine administration is not recommended to patients with ferritin levels >500 ng/mL, although each patient should be individually assessed.
- Results from the Dialysis Patients' Response to IV Iron with elevated ferritin (DRIVE) study suggested that iron therapy may lead to increases in hemoglobin levels and reduced ESA requirements even in patients with serum ferritin levels in excess of 500 µg/L.[14]

## What Iron Therapeutic Options Should Be Considered?

- There are a number of options available for treatment including oral iron which can be tried but many patients find intolerable as well as the concern for limited absorption.
- Multiple intravenous iron preparations available include ferumoxytol, iron sucrose, ferric gluconate in sucrose complex, ferric carboxymaltose, and low-molecular-weight iron dextran.
- All of these products are equally effective in treating iron deficiency.[15]

## Is High-Dose IV Iron Safe?

- The Proactive IV Iron Therapy in Haemodialysis Patients (PIVOTAL) trial compared 400 mg monthly of IV iron sucrose administered proactively unless the ferritin was > 700 ng/ml or the transferrin saturation was > 40% to low dose iron sucrose, 0-400 mg monthly for ferritin < 200 ng/ml or transferrin saturation less than 20%.
- The proactive, high dose regimen was found to be non-inferior for the primary endpoint of a composite of nonfatal myocardial infarction, nonfatal stroke, hospitalization for heart failure, or death, assessed in a time-to first-event analysis.
- The high-dose regimen resulted in a reduction in the dose of erythropoiesis-stimulating agents required, no difference in infection rates, a lower rate of hospitalization for heart failure and a lower rate of transfusion.[17]

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