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www.reachmd.com  
info@reachmd.com  
(866) 423-7849

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## Optimizing Iron Deficiency Management in CKD: IV Iron Replacement Therapy Amid the Latest KDIGO Guidelines

### Announcer:

You're listening to ReachMD. This activity, titled "Optimizing Iron Deficiency Management in CKD: IV Iron Replacement Therapy Amid the Latest KDIGO Guidelines" is provided by Medtelligence.

### Dr. Neuen:

Hello, everyone. My name is Brendon Neuen. I'm a nephrologist and associate professor of medicine at Royal North Shore Hospital in Sydney, Australia, and I'm program lead of the Renal Division at the George Institute for Global Health. I'm delighted to be here today talking to you about some of the new updates in the KDIGO 2026 Anemia in CKD Guidelines.

I'm going to mainly focus today on some of the new recommendations in these guidelines with respect to the management of people with anemia and iron deficiency: when we should be screening for iron deficiency, how should we be using iron, what are the thresholds for using iron, and what are their potential benefits on clinical outcomes for patients with kidney disease?

So what I'll start off by saying and addressing is why do we need a new guideline? Well, the last KDIGO guidelines for anemia in kidney disease were updated in 2012, so that's 14 years ago. And we have 14 years of new evidence to incorporate in these guidelines.

So the first thing I'll talk about is how common is anemia and how common is iron deficiency in people with kidney disease? Well, when we look through the KDIGO guidelines, anemia is defined based on the WHO definition, which is a hemoglobin of less than 130 g/L in men and less than 120 g/L in women. And we all know that anemia is incredibly common in people with kidney disease, affecting approximately a third of those with non-dialysis CKD, and this increases in prevalence to almost 50% in people with more advanced forms of kidney disease. At the same time, we know that iron deficiency is even more prevalent.

So this is a very common problem, but it's also a very important problem, because we also know from epidemiological and registry data that iron deficiency and anemia are both associated with reduced quality of life, increased risk of cardiovascular events, increased risk of hospitalizations, cognitive impairment, and of course a higher risk of transfusion requirements.

But what we also know from registry data over the last few years is that despite knowing how common iron deficiency is, despite knowing how common anemia is, anemia and iron deficiency remain undertreated before dialysis initiation. So this underscores the importance of identifying patients with iron deficiency and anemia, getting the diagnosis right as the first essential step in treating and improving outcomes for these individuals.

So importantly, the guidelines make new recommendations about how often we should be screening for iron deficiency and for anemia in people with kidney disease, and there are a number of recommendations and practice points in the updated guidelines. What the guidelines now suggest is that patients should be screened for iron deficiency and anemia at referral, regularly during follow-up, and whenever symptoms suggest the presence of anemia.

And the guidelines also outline minimum testing frequencies by CKD stage. But of course, more frequent testing may be warranted if patients are on EPO, if they're on a HIF stabilizer, if hemoglobin is above target or below target and we're adjusting those agents, or if

CKD is progressing rapidly.

The guidelines also recommend a standard screening set for anemia and iron deficiency, which includes a full blood count, reticulocyte count, as well as iron studies. Of course, it's important to remember that we should always consider and evaluate blood loss, occult blood loss particularly from the gastrointestinal tract in people with iron deficiency of uncertain cause, with an appropriate referral to gastroenterology services as required.

Also outlined in the guidelines are recommendations about if anemia is present and iron deficiency isn't, that a broader panel might be considered. That might include testing for B12, folate, a hemolysis screen, CRP, a myeloma screen with a serum protein electrophoresis and immunofixation, as well as TSH and fecal occult blood. So these are important practical recommendations that we can take back to the clinic every day.

The overall point here that the guidelines emphasize is that we should avoid reflexively attributing all anemia to kidney disease.

The guidelines also use new terminology for iron deficiency and retires the old terminology that we're all probably familiar with. So what we used to call absolute iron deficiency, where patients may have low ferritin and low TSATs reflecting depleted stores and reduced circulating iron, is now called systemic iron deficiency. What we previously referred to as functional iron deficiency, where patients may have normal or elevated ferritin levels but low TSATs reflecting inflammation-driven iron sequestration via elevated hepcidin, is now referred to as iron-restricted erythropoiesis.

Why does this matter? Well, the new terms more accurately describe the underlying pathophysiology, which is particularly relevant in kidney disease, where inflammation is nearly universal in our patients. Iron-restricted erythropoiesis explains why iron supplementation can still raise hemoglobin and reduce ESA requirements even when ferritin isn't low. And what the guidelines and the evidence is moving towards are that TSATs are emerging as a more informative marker of iron stores in this state where ferritin alone is unreliable because it's an acute-phase reactant. We've always known this, but it's nice to see this incorporated into the guidelines and included under the term of iron-restricted erythropoiesis.

So what do the guidelines say about treating iron deficiency in people with non-dialysis CKD? What the 2026 guidelines recommend now, and this is a 2D recommendation, is that we should initiate iron in patients with non-dialysis CKD who are anemic if they have a ferritin less than 100 ng/L and TSATs less than 40% or if their ferritin levels are between 100 and 300 and TSATs are less than 25%. This evidence is based on small, randomized trials, and that's why the recommendation is a 2D recommendation, as there's not a lot of strong evidence for clinical outcomes for specific ferritin and TSAT values at which to initiate iron.

The guidelines also provide a pragmatic approach to withholding iron, suggesting that iron should be withheld if ferritin levels are greater than 700 or TSATs are greater than 40%. This is a practice point aligned, again, with contemporary randomized controlled trials, including the PIVOTAL trial. Importantly, this recommendation in non-dialysis CKD also applies to kidney transplant recipients and to patients who are treated with peritoneal dialysis.

One final important point from the guidelines, and this is the departure from the 2012 guidelines, is there is a practice point that states even in the absence of anemia, profound iron deficiency, defined as a ferritin of less than 30 and TSATs of less than 20%, may warrant treatment given iron's important biological roles beyond erythropoiesis, including for mitochondrial function in cardiac and skeletal muscle, as well as potential effects on cognitive function.

Now, in terms of route of administration, the guidelines suggest that either oral or IV iron may be used in patients with non-dialysis CKD based on patient preferences and values, the degree of iron deficiency, efficacy, tolerability, availability, and cost. Neither route is formally preferred. However, what the guidelines do also acknowledge is we have very limited evidence in this space. There are very few, if any, adequately powered randomized controlled trials assessing the effects of IV iron on clinical outcomes in non-dialysis CKD. And most of the potential benefits of iron in this population are extrapolated from if there are effects on hemoglobin and therefore quality of life. And so this is an important research gap, and this is a space where well-designed randomized controlled trials are urgently needed and where ongoing efforts to design and fund such trials are really relevant to the care of kidney disease patients going forward.

How about managing iron deficiency and administering iron in the dialysis setting? Now, these recommendations in the 2026 guidelines are largely based on the PIVOTAL trial. They recommend initiating iron in patients on dialysis if their ferritin level was less than 500 and

TSATs are less than 30%. This applies regardless of whether patients are receiving ESAs, HIF stabilizers, or neither. They recommend IV as the preferred route over oral iron in dialysis patients to reduce pill burden and achieve more rapid and reliable iron repletion.

And the guidelines also importantly recommend a proactive approach whereby we administer iron regularly, at regular intervals, to maintain stable iron status rather than waiting for iron stores to fall below a threshold.

The guidelines, also based on PIVOTAL, recommend withholding iron in dialysis patients if TSATs are greater than 40% or ferritin levels are greater than 700.

So in summary, putting together everything in the 2026 KDIGO anemia guidelines with respect to iron deficiency, what the guidelines tell us are clear: we should screen patients at appropriate intervals using full blood count, reticulocyte count, and iron stores. There are new recommendations on how frequently that should occur, being at least annually in patients with stage 3 CKD, twice yearly in patients with stage 4 CKD, and 3-monthly in patients with stage 5 CKD, including those on dialysis.

We know that if patients have anemia but do not have iron deficiency, the guidelines provide additional criteria and guidance for how to work those patients up to identify other causes of anemia. The guidelines also apply new nomenclature to characterize iron deficiency, including changing absolute iron deficiency to systemic iron deficiency and changing functional iron deficiency to iron-restricted erythropoiesis, which better reflects the underlying pathobiology of the disease.

There are updated guidance on thresholds on when to treat with intravenous or oral iron, with TSATs emerging as the most reliable guide, rather than ferritin alone, in the presence of inflammation, which is common in people with kidney disease. And the choice of either oral iron or IV iron will depend on patient preferences, availability, cost in the non-dialysis setting, but intravenous iron is preferred in dialysis patients.

Importantly, for patients with profound iron deficiency, even in the absence of anemia, the guidelines support considering treatment in patients based on the non-erythropoietic potential benefits of IV iron.

Thanks very much for joining me today as we walked through some of the major updates in the KDIGO 2026 anemia guidelines. Thank you for joining us, and I look forward to discussing future guideline updates and the care of patients with kidney disease with you in the future.

**Announcer:**

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