



Indian Health Service
National Pharmacy & Therapeutics Committee
Formulary Brief: Nutritional Supplements in Hematology: Iron
-February 2016-



Background:

At the February 2016 Indian Health Service (IHS) National Pharmacy & Therapeutics Committee (NPTC) meeting, the committee reviewed the role of iron in treating iron deficiency. Prior to this meeting, the IHS National Core Formulary (NCF) did not include any iron products. As a result of the clinical and pharmacoeconomic review, the **NPTC added an oral iron supplement (any product)** to the NCF.

Iron deficiency (ID), the most common nutritional deficiency worldwide, is defined as a reduction in iron stores that persists without progression or precedes overt iron deficiency anemia (IDA). IDA is defined as low levels of iron associated with anemia and includes the presence of microcytic, hypochromic red cells. Of the approximately 10 million people in the US with ID, about 50% have IDA^{1,2}. It is most prevalent in women of childbearing age, followed by children under the age of 3 years. Iron can be replete through diet, oral or IV supplementation.

Discussion:

There are many reviews of iron in the treatment of both ID and IDA. A 2011 Cochrane review looked at treatments for IDA in pregnancy. The review assessed effects of different treatments for IDA in pregnancy on maternal and neonatal morbidity and mortality. Reviewers were unable to balance benefits and harms of different treatments for different levels of anemia. They could not conclude if treatment of mild anemia is beneficial and where unclear as to which treatments are safer and more effective in treating moderate to severe anemia³.

A Cochrane review in 2015 evaluated intermittent versus daily oral iron supplementation. Reviewers found no differences between groups in anemia at term or IDA at term. The group using intermittent supplementation group was less likely to report side effects (average RR 0.56, 95% CI: 0.37 to 0.84). No significant differences were found between treatment groups in infant outcomes of birthweight, premature birth, nor neonatal death. The authors concluded that intermittent iron could be considered a feasible strategy to prevent gestational anemia⁴.

In 2015, another Cochrane review assessed treatment for postpartum IDA. This review evaluated different treatment modalities for treating IDA including oral iron, intravenous (IV) iron, and IV iron plus oral iron. Many of the studies were of low quality and investigators could make no clear conclusion regarding the efficacy of interventions. It was noted that IV iron was superior to oral regarding gastrointestinal (GI) side effects, but more evidence is needed related to anaphylaxis and cardiac events⁵.

A 2014 Cochrane review studying anemia in adults without chronic kidney disease (CKD) suggested oral iron might decrease the proportion of transfusions, but not mortality. It may be useful in adults who can tolerate the adverse effects. Intravenous iron has a modest increase in hemoglobin levels when compared with oral iron, but there is no evidence of clinical benefit over oral iron. Investigators found no evidence to suggest advantage of one iron preparation or regimen over another.

In 2012, a Cochrane review compared oral iron to IV iron in children and adults with CKD. Only 1 of the 28 studies reviewed included children on hemodialysis and only 1 study included peritoneal dialysis. Data from this review support the use of IV iron for hemodialysis patients to increase iron stores. Hemoglobin was significantly increased with IV compared to oral iron (mean difference [MD] 0.90 g/dL, 95% CI: 0.44 to 1.97), as was ferritin (MD 2.43 g/dL, 95% CI: 188 to 2997). There is insufficient evidence to determine if benefits of iron therapy exceed harm in all patients with CKD⁷.

The National Institute for Health and Clinical Excellence published updated guidelines in 2015 for managing anemia in CKD. It is recommended to offer iron therapy for those who are ID and not using erythropoietin stimulating agents (ESA). Oral therapy is appropriate for those not on hemodialysis (HD).

Intravenous iron should be offered to those on HD and those who have failed an adequate trial of oral. Intravenous therapy should be offered to those using ESA, except for children not on HD⁸.

The U.S. Preventive Services Task Force (USPSTF) issued an updated recommendation statement on screening for IDA and iron supplementation in pregnant women in 2015. This statement applies to U.S. population with no symptoms of IDA. The USPSTF did not make recommendations in favor of or against screening for ID nor for providing iron supplementation as they found insufficient evidence for both. This is contradictory to numerous organizational recommendations including the Institute of Medicine recommendation to screen for IDA in each trimester (which was based on 2006 USPSTF recommendation), the American College of Obstetrics and Gynecology which recommends screening all pregnant women and treating those with IDA, and the Centers for Disease Control and Prevention recommendation from 1998 recommending screening and initiating low dose iron supplementation at first prenatal visit².

The British Society for Gastroenterology published guidelines in 2011 for Western gastroenterologists and GI surgeons. This guideline supports the use of oral iron (ferrous sulfate 200mg po bid) to treat IDA and replenish iron stores. They recommend IV iron for intolerance or inadequate response to oral iron. They also recommend oral iron to treat ID without anemia⁹.

Iron deficiency is common in both inflammatory bowel disease (IBD) and celiac disease. For IBD, iron therapy is recommended when IDA is present. Intravenous iron is preferred, as non-absorbed ferrous iron has the potential to worsen IBD symptoms. Iron supplementation is not recommended in celiac disease^{10,11}.

Findings:

The **NPTC added an oral iron supplement (any product)** to the National Core Formulary. Consideration should be given for the addition of IV iron products to local P&T formularies, where applicable, as it does have a defined role in the treatment of iron deficiency.

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](#).

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