

**SOUTH AFRICAN PRIMARY HEALTHCARE LEVEL ESSENTIAL MEDICINES LIST
CHAPTER 3: NUTRITION AND ANAEMIA
NEMLC RECOMMENDATIONS FOR MEDICINE AMENDMENTS (2020)**

Medicine amendment recommendations, with supporting evidence and rationale are listed below.

Kindly review the medicine amendments in the context of the complete chapter for nutrition and anaemia.

Note: The PHC chapter has been updated to align to previous NEMLC recommendations as well as the recent NEMLC-approved Adult Hospital Level STGs and EML, 2019 edition.

SECTION	MEDICINE / MANAGEMENT	ADDED/DELETED/AMENDED
3.1.1 Anaemia, iron deficiency		
- <i>Treatment: Adults</i>	Ferrous sulfate, oral	Retained and dosing amended to include dosing (including when there is poor tolerance)
	Ferrous fumarate, oral	Retained and dosing amended to include dosing (including when there is poor tolerance)
- <i>Prophylaxis: Pregnant women</i>	Iron anaemia deficiency (with iron supplements)	Cross referenced to section 6.4.1: Antenatal supplements

3.1.1 ANAEMIA, IRON DEFICIENCY

Treatment: Adults

Ferrous sulfate, oral: retained and dosing amended to include dosing when there is poor tolerance (e.g. epigastric pain, nausea, vomiting and constipation)

Ferrous fumarate, oral: retained and dosing amended to include dosing when there is poor tolerance (e.g. epigastric pain, nausea, vomiting and constipation)

Poor tolerance to oral iron supplements

Evidence for alternate dosing of oral iron supplements for treating iron deficiency anaemia is limited and of low quality: underpowered, may not be generalisable to the local setting, study design provides pharmacokinetic and pathophysiological information rather than clinical meaningful inferences.

Hepcidin, which regulates body iron homeostasis was shown to increase with increased dosing of oral iron decreasing iron absorption: 24 hours after doses ≥ 60 mg, serum hepcidin increased by 35%, $p < 0.01$ and fractional iron absorption decreased by 45%, $p < 0.01$.¹

Poor tolerance: Pragmatic option would be to recommend alternate day dosing of iron if daily iron cannot be tolerated.

Recommendation: Alternate day dosing of oral iron recommended for treatment of iron deficiency anaemia, where daily dosing is poorly tolerated.

Rationale: Pragmatic option provided for poor tolerance of daily oral iron supplements as alternate day dosing. Limited evidence suggests that hepcidin levels increase with increasing doses of oral iron, and the alternate day dosing regimen recommended to minimise use of parenteral iron in patients who cannot tolerate or who are not responding to oral iron supplements.

Level of Evidence: III Pharmacokinetic²/pharmacodynamics studies, Expert opinion

Refer to the previous PHC recommendations, accepted by NEMLC at the meeting of 14 December 2017 – see below:

PHC Obstetrics and Gynaecology NEMLC report of 14 December 2017:

Iron: (Refer to the medicine review: *Intermittent iron supplementation in pregnancy, 6 November 2017*).

¹ Moretti D, Goede JS, Zeder C, Jiskra M, Chatzinakou V, Tjalsma H, Melse-Boonstra A, Brittenham G, Swinkels DW, Zimmermann MB. Oral iron supplements increase hepcidin and decrease iron absorption from daily or twice-daily doses in iron-depleted young women. *Blood*. 2015 Oct 22;126(17):1981-9. <https://www.ncbi.nlm.nih.gov/pubmed/26289639>

² Stoffel NU, Cercamondi CI, Brittenham G, Zeder C, Geurts-Moespot AJ, Swinkels DW, Moretti D, Zimmermann MB. Iron absorption from oral iron supplements given on consecutive versus alternate days and as single morning doses versus twice-daily split dosing in iron-depleted women: two open-label, randomised controlled trials. *Lancet Haematol*. 2017 Nov;4(11):e524-e533. <https://www.ncbi.nlm.nih.gov/pubmed/29032957>

Recommendation: Based on the evidence review, the PHC Committee was of the opinion that intermittent iron is not appropriate as antenatal supplementation for all pregnant women. Iron supplementation in pregnancy should be recommended as daily iron dosing. However, if iron is poorly tolerated, intermittent iron supplementation should be considered as an alternative.
Rationale: Current low quality evidence suggests that intermittent iron supplementation is as efficacious as daily dosing in pregnant women. Furthermore, local prevalence study estimates that 30-40% of pregnant women have anaemia.
Level of Evidence: I Systematic review³, Prevalence study⁴

Possible causes of treatment failure:

Following text was added to the STG, aligned with the Adult Hospital Level STGs and EML, 2019 edition:

Consider the following if there is failure to respond to iron therapy:

- » non-adherence,
- » continued blood loss,
- » wrong diagnosis,
- » malabsorption, or
- » mixed deficiency; concurrent folate or vitamin B₁₂ deficiency.

Level of Evidence: III Guidelines⁵

Prophylaxis: Pregnant women

A cross-reference to section 6.4.1: Antenatal supplements, was added that guides on iron supplementation during pregnancy.

³ Pena-Rosas JP, De-Regil LM, Gomez Malave H, Flores-Urrutia MC, Dowswell T. Intermittent oral iron supplementation during pregnancy. The Cochrane database of systematic reviews. 2015(10):CD009997. <https://www.ncbi.nlm.nih.gov/pubmed/26482110>

⁴ Tunkyi K, Moodley J. Prevalence of anaemia in pregnancy in a regional health facility in South Africa. S Afr Med J. 2015;106(1):101-4. <https://www.ncbi.nlm.nih.gov/pubmed/26792317>

⁵ Adult Hospital Level STGs and EML, 2019 edition