

CADTH Reference List

Iron Isomaltoside for Anemia Due to Pregnancy, Menorrhagia, or Other Gynecological Conditions

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Key Messages

- No evidence was found regarding the clinical effectiveness of iron isomaltoside for non-pregnant patients with menorrhagia or other gynecologic indications.
- One non-randomized study was identified regarding the clinical effectiveness of iron isomaltoside for patients with anemia related to pregnancy.
- Two randomized controlled trials were identified regarding the clinical effectiveness of iron isomaltoside for postpartum patients with anemia.

Research Questions

1. What is the clinical effectiveness of iron isomaltoside for non-pregnant patients with menorrhagia or other gynecologic indications?
2. What is the clinical effectiveness of iron isomaltoside for patients with anemia related to pregnancy?
3. What is the clinical effectiveness of iron isomaltoside for postpartum patients with anemia?

Methods

Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including MEDLINE, Embase, the Cochrane Database of Systematic Reviews, the international HTA database, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search strategy comprised both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were iron isomaltoside, iron deficiency anemia, menorrhagia, pregnant patients, postpartum patients, and patients with other gynecologic indications. No filters were applied to limit the retrieval by study type. Comments, newspaper articles, editorials, conference abstracts, and letters were excluded. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 01, 2016 and November 15, 2021. Internet links were provided, where available.

Selection Criteria and Summary Methods

One reviewer screened literature search results (titles and abstracts) and selected publications according to the inclusion criteria presented in Table 1. Full texts of study publications were not reviewed. The Overall Summary of Findings was based on information available in the abstracts of selected publications.

Table 1: Selection Criteria

Criteria	Description
Population	Q1: Non-pregnant patients with menorrhagia and other gynecologic indications Q2: Patients with anemia related to pregnancy Q3: Postpartum patients with anemia due to any reason (e.g., postpartum hemorrhage patients, post, pre, peri-operative c-section patients with borderline hemoglobin levels)
Intervention	IV iron isomaltoside (any dosage; Monofer, Monoferric, ferric derisomaltose)
Comparator	IV iron sucrose (e.g., Venofer); injected iron dextran; IV sodium ferric gluconate (e.g., Ferrlecit); oral iron medications (e.g., Ferrous gluconate [e.g., Fergon, Ferralet and Simron], Ferrous fumarate [e.g., Hemocyte, Ferretts Iron, Ferrocite], Ferrous sulphate [e.g., FeroSul, Feosol Original, Iron Sulphate, Fer-In-Sol], Polysaccharide Iron Complex Oral, Alpha Heme Iron [e.g., OptiFer], Heme Iron polypeptide [e.g., Proferrin])
Outcomes	Q1 to Q3: Clinical effectiveness (e.g., hemoglobin levels, ferritin levels, time to recovery of hemoglobin or ferritin level, iron or transferrin saturation, serum iron levels, safety, maternal and fetal outcomes)
Study designs	Health technology assessments, systematic reviews, randomized controlled trials, non-randomized studies

Results

Three relevant references were identified for this report.¹⁻³ One non-randomized study was identified regarding the clinical effectiveness of iron isomaltoside for patients with anemia related to pregnancy.³ Two randomized controlled trials were identified regarding the clinical effectiveness of iron isomaltoside for postpartum patients with anemia.^{1,2} No relevant health technology assessments or systematic reviews were identified.

Additional references of potential interest that did not meet the inclusion criteria are provided in Appendix 1.

Overall Summary of Findings

One non-randomized study³ assessed the clinical effectiveness of patients with anemia related to pregnancy, comparing Monofer (IV iron isomaltoside) to Venofer (IV iron sucrose) in pregnant patients. The authors reported no severe drug reactions in either group, and that a small number of patients in the Monofer group experienced flushing, headaches, and vomiting.³

Two randomized controlled trials^{1,2} assessed the clinical effectiveness of IV iron isomaltoside compared to oral iron in women following postpartum hemorrhage. One study² was a subanalysis limited to patients with severe fatigue following the hemorrhage. Both studies^{1,2} reported that a single-dose IV infusion was associated with improvements in physical fatigue, depression, hematological parameters, and iron parameters; both also reported no serious adverse events.

No relevant literature was found regarding the clinical effectiveness of iron isomaltoside for non-pregnant patients with menorrhagia or other gynecologic indications; therefore, no summary can be provided.

References

Health Technology Assessments

No literature identified.

Systematic Reviews and Meta-analyses

No literature identified.

Randomized Controlled Trials

1. Holm C, Thomsen LL, Norgaard A, Langhoff-Roos J. Single-dose intravenous iron infusion or oral iron for treatment of fatigue after postpartum haemorrhage: a randomized controlled trial. *Vox Sang.* 2017 Apr;112(3):219-228. [PubMed](#)

Sub-Analysis of a Randomized Controlled Trial

2. Holm C, Thomsen LL, Langhoff-Roos J. Intravenous iron isomaltoside treatment of women suffering from severe fatigue after postpartum hemorrhage. *J Matern Fetal Neonatal Med.* 2019 09;32(17):2797-2804. [PubMed](#)

Non-Randomized Studies

3. Ashaye T, Umer S, Zill-E-Huma R. An observational study in the UK comparing the safety and cost-effectiveness of intravenous iron preparations Monofer to Venofer for the treatment of iron deficiency anaemia in pregnancy. *ARC J Gynecol Obstet.* 2021;6(1):01-09.

Appendix 1: References of Potential Interest

Previous CADTH Reports

4. Screening and treatment of obstetric anemia: a review of clinical effectiveness, cost effectiveness, and guidelines. (*CADTH rapid response report: summary with critical appraisal*). Ottawa (ON): CADTH; 2019 Dec: <https://www.cadth.ca/sites/default/files/pdf/htis/2019/RC1216%20-%20Screening%20and%20treatment%20of%20obstetric%20anemia%20Final.pdf>. Accessed 2021 Nov 17.

Health Technology Assessments

Unclear Intervention – Not Specific to Iron Isomaltoside

5. Lattepi NM. Intravenous iron for iron deficiency anaemia. Putrajaya (MY): Health Technology Assessment Section (MaHTAS), Ministry of Health Malaysia; 2019: https://www.moh.gov.my/index.php/database_stores/attach_download/348/341. Accessed 2021 Nov 17.
See: Efficacy and effectiveness (p.5-6); 5.1.1.5 Pregnancy (p.23); 5.1.1.6 Postpartum (p.24)

Systematic Reviews and Meta-analyses

Unclear Intervention – Not Specific to Iron Isomaltoside

6. Rogozińska E, Rogozinska E, Daru J, Nicolaidis M, et al. Iron preparations for women of reproductive age with iron deficiency anaemia in pregnancy (FRIDA): a systematic review and network meta-analysis. *Lancet Haematol*. 2021 Jul;8(7):e503-e512. [PubMed](#)
7. Govindappagari S, Burwick RM. Treatment of Iron Deficiency Anemia in Pregnancy with Intravenous versus Oral Iron: Systematic Review and Meta-Analysis. *Am J Perinatol*. 2019 Mar;36(4):366-376. [PubMed](#)
8. Lewkowicz AK, Gupta A, Simon L, et al. Intravenous compared with oral iron for the treatment of iron-deficiency anemia in pregnancy: a systematic review and meta-analysis. *J Perinatol*. 2019 Apr;39(4):519-532. [PubMed](#)
9. Qassim A, Grivell RM, Henry A, Kidson-Gerber G, Shand A, Grzeskowiak LE. Intravenous or oral iron for treating iron deficiency anaemia during pregnancy: systematic review and meta-analysis. *Med J Aust*. 2019 Oct;211(8):367-373. [PubMed](#)
10. Sultan P, Bampoe S, Shah R, et al. Oral vs intravenous iron therapy for postpartum anemia: a systematic review and meta-analysis. *Am J Obstet Gynecol*. 2019 Jul;221(1):19-29 e13. [PubMed](#)

Randomized Controlled Trials

Alternative Comparator – Red Blood Cell Transfusion

11. Holm C, Thomsen LL, Norgaard A, Langhoff-Roos J. Single-dose intravenous iron infusion versus red blood cell transfusion for the treatment of severe postpartum anaemia: a randomized controlled pilot study. *Vox Sang*. 2017 Feb;112(2):122-131. [PubMed](#)

Alternative Outcome – Iron Concentration in Breast Milk

12. Holm C, Thomsen LL, Norgaard A, Markova V, Michaelsen KF, Langhoff-Roos J. Iron concentration in breast milk normalised within one week of a single high-dose infusion of iron isomaltoside in randomised controlled trial. *Acta Paediatr*. 2017 02;106(2):256-260. [PubMed](#)

Protocol

13. Markova V, Hansen R, Thomsen LL, Pinborg A, Moos T, Holm C. Intravenous iron isomaltoside versus oral iron supplementation for treatment of iron deficiency in pregnancy: protocol for a randomised, comparative, open-label trial. *Trials*. 2020 Aug 26;21(1):742. [PubMed](#)
14. University Medical Centre Ljubljana. NCT03957057: Intravenous Iron Carboxymaltose, Isomaltoside and Oral Iron Sulphate for Postpartum Anemia. *ClinicalTrials.gov*. Bethesda (MD): U.S. National Library of Medicine; 2020 Sep: <https://clinicaltrials.gov/ct2/show/NCT03957057>. Accessed 2021 Nov 17.

Non-Randomized Studies

Alternative Comparator – No Treatment

15. Wesstrom J. Safety of intravenous iron isomaltoside for iron deficiency and iron deficiency anemia in pregnancy. *Arch Gynecol Obstet*. 2020 05;301(5):1127-1131. [PubMed](#)

Review Articles

16. Daniilidis A, Panteleris N, Vlachaki E, Breyman C, Assimakopoulos E. Safety and efficacy of intravenous iron administration for uterine bleeding or postpartum anaemia: a narrative review. *J Obstet Gynaecol*. 2016 May 19;38(4):443-447. [PubMed](#)