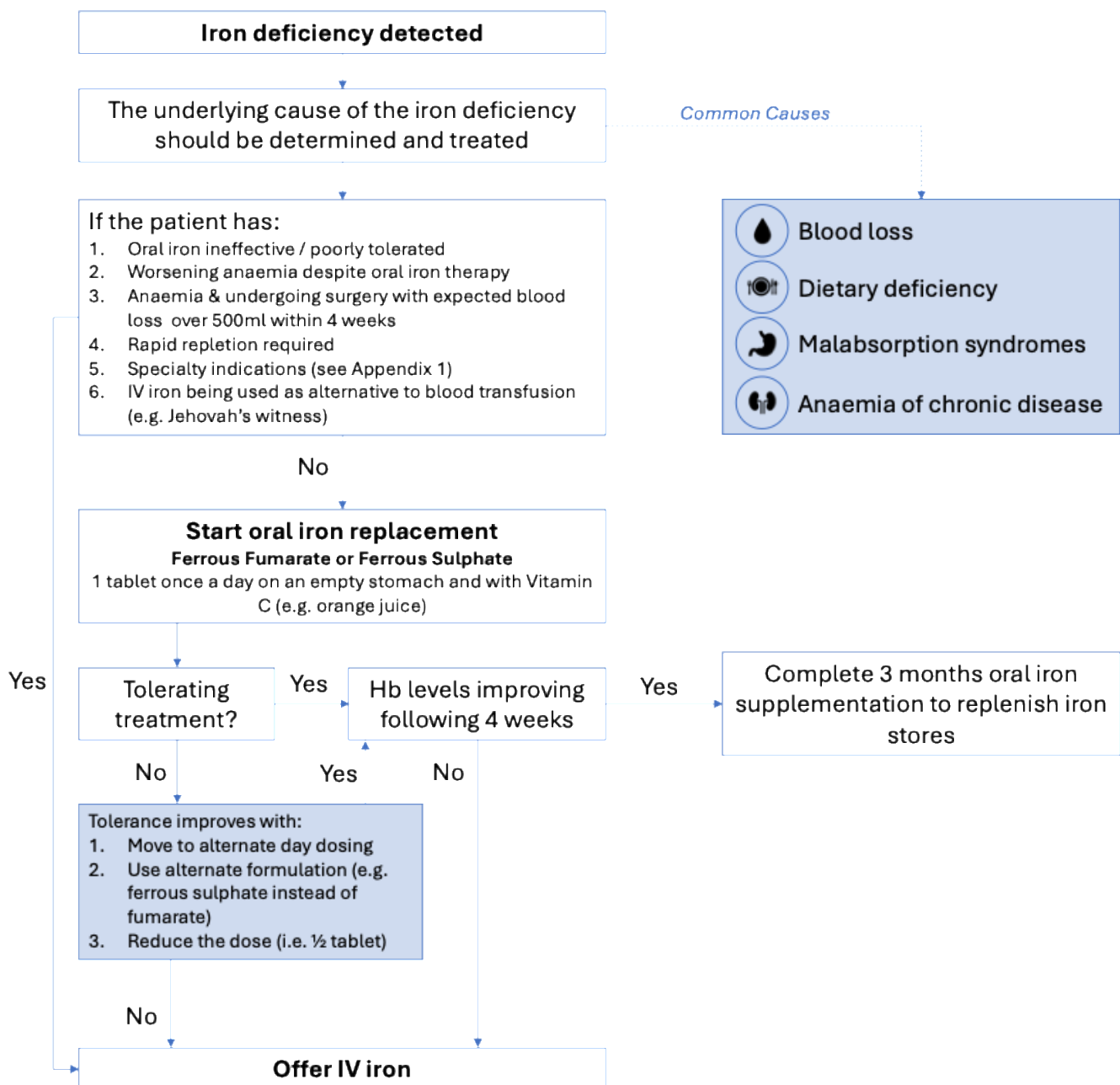


*This Medicines Information Leaflet is produced locally to optimize the use of medicines by encouraging prescribing that is safe, clinically appropriate and cost-effective to the NHS.*

## Iron Replacement

### Assessment & Management of Iron Deficiency



## Contents

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## Definitions

Condition	Definition	Clinical Features / comments
Depletion of iron stores	<ul style="list-style-type: none"> <li>• ↓Ferritin</li> </ul>	<ul style="list-style-type: none"> <li>• Nil</li> </ul>
Iron deficiency	<ul style="list-style-type: none"> <li>• Ferritin less than 30 mcg/L</li> <li>• ↓Transferrin saturation, Ret-Hb</li> </ul> <p>NB: Different thresholds used in guidance for heart failure, renal, oncology – see <a href="#">appendix</a>.</p>	<ul style="list-style-type: none"> <li>• Common: Fatigue, dyspnoea, headaches, palpitations, light-headedness, worsening angina, limb claudication, brain fog, reduced performance at work or hair loss.</li> <li>• Less common: Itch, tongue pain, angular stomatitis, pica, restless legs, koilonychia, mood disorder.</li> </ul>
Iron deficiency anaemia (IDA)	<p>As per iron deficiency, plus Hb under threshold:</p> <ul style="list-style-type: none"> <li>• 130g/L: adult men</li> <li>• 120g/L: non-pregnant women</li> </ul>	<p>Late feature of iron deficiency</p> <p>NB: Threshold of 130g/L also used for pre-operative assessment of nonpregnant women</p>
Functional iron deficiency	<ul style="list-style-type: none"> <li>• Ferritin &amp; CRP often raised</li> <li>• Transferrin saturation less than 16%</li> <li>• ↓Ret-Hb, Hb</li> </ul>	<p>Chronic inflammatory states sequester iron &amp; reduce iron absorption/transport</p>

NB: Serum iron is not useful for assessment of total body iron stores.

## Management

- Confirm iron deficiency with iron studies and assess for vitamin B12 & folate deficiency.
- Identify and treat underlying cause, but don't delay treatment.
- If no clear cause identified:
  - Test tissue transglutaminase antibody levels
  - Urinalysis (for microscopic haematuria)
  - Consider OGD/colonoscopy
- Specialty Specific Guidelines are detailed in [appendix](#).

### Oral Iron Replacement (Preferred)

Recommended regimens	Ferrous Fumarate 210mg (70mg iron) OR Ferrous Sulphate 200mg (65mg iron) Daily (or alternate days); see <a href="#">flowchart</a> for administration details
Alternatives	Ferrous fumarate syrup 140mg/5ml (45mg/5ml iron) is also available. Non-formulary preparations available on case-by-case basis
Not recommended	Over-the-counter (OTC) supplements; these do not contain sufficient iron & may contain ingredients that reduce absorption.

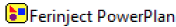
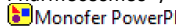
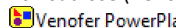
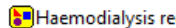
### Common or important interactions:

Reduced absorption of drug	<ul style="list-style-type: none"> <li>• Tetracyclines</li> <li>• Quinolones</li> <li>• Bisphosphonates</li> <li>• Zinc</li> </ul>
Reduced absorption of iron	<ul style="list-style-type: none"> <li>• Zinc or magnesium salts (for example in antacids).</li> <li>• Calcium (for example in milk and dairy products).</li> <li>• Tannins (for example in tea, coffee, and cocoa).</li> <li>• Phytates (present in cereal grains, legumes, nuts, and seeds).</li> </ul>
Interactions	<ul style="list-style-type: none"> <li>• Methyldopa — the antihypertensive effect can be reduced.</li> <li>• Levodopa — the bioavailability may be reduced.</li> <li>• Levothyroxine — the effects of levothyroxine may be reduced.</li> <li>• Penicillamine — the absorption reduced up to 66%.</li> </ul>

### Intravenous Iron

#### Administration

- Refer to [Medusa Guidelines](#) for details on how to prepare IV iron for infusion.
- Please prescribe, request, supply and administer as early as possible. There is usually no need to request or supply overnight (i.e. between 10pm and 8am)
- To avoid overdose, a maximum of one dose will be supplied by Pharmacy at any one time.

Preparation	Doses	Administration
Ferric carboxymaltose (Ferinject®) - Preferred/First line 	500mg 1g	<ul style="list-style-type: none"> <li>• Infusion: 20mg/kg (maximum 1g).</li> <li>• Administer over 15 minutes</li> <li>• Follow up doses should be given 1 week later.</li> </ul>
Ferric derisomaltose (Ferric Derisomaltose Pharmocosmos®) 	500mg 1g 1.5g 2g	<ul style="list-style-type: none"> <li>• Infusion: 20mg/kg (maximum 2g; typically 1g).</li> <li>• Administer over 15 minutes (30m if dose is greater than 1g)</li> <li>• Follow up doses should be given 1 week later.</li> </ul> NB: Used only in patients who experience hypophosphataemia with Ferinject®.
Iron sucrose (Venofer®) 	100mg 200mg	<ul style="list-style-type: none"> <li>• Infusion: Up to 200mg</li> <li>• Administer over 30 minutes</li> </ul> NB: May be administered up to 3x/week
Ferric derisomaltose (Diafer®) Renal only 	200mg	Maximum weekly dose of 1g  Used only for patients receiving in-centre haemodialysis. Can be administered as a bolus or into the venous limb of the dialyser.

**Contraindications & Cautions**

Contraindication	Caution
<ul style="list-style-type: none"> <li>Allergic to IV iron preparations</li> <li>Iron overload syndrome</li> <li>Pregnant patients in the first trimester</li> <li>Children less than 14 years.</li> <li>Venofer® is contraindicated for patients with atopy (asthma, eczema, hayfever).</li> </ul>	<ul style="list-style-type: none"> <li>Liver dysfunction</li> <li>Low phosphate (occurs with Ferinject® more than Ferric derisomaltose)</li> <li>Active infection, unless clinically improving (Patients with chronic infection may have suppressed erythropoiesis).</li> <li>Ferinject® and Ferric Derismaltose Pharmocosmos® are cautioned in patients with atopy.</li> </ul>

**Monitoring**

<b>During infusion</b>	<ul style="list-style-type: none"> <li>Blood pressure: before, during &amp; after administration</li> <li>Vascular access: monitor for irritation/extravasation</li> <li>After infusion: monitor for 10-15 minutes (30 mins for Ferric derisomaltose)</li> </ul>
<b>To assess effect</b>	<ul style="list-style-type: none"> <li>Hb: 4-6 weeks after last dose. Target is a Hb increase of ~20g/L.</li> <li>Iron indices will be elevated after IV iron for 4 weeks.</li> </ul>
<b>Other</b>	<ul style="list-style-type: none"> <li>Serum phosphate: Low phosphate reported with Ferinject®, less so with other formulations. Monitor phosphate in patients with risk factors for hypophosphataemia or who receive multiple administrations.</li> </ul>

**Adverse Drug Reactions**

- See [BNF](#) for details.
- True anaphylaxis is rare. Infusion reactions to IV iron are common and can usually be managed by stopping and slowing the infusion rate.

**Extravasation injury & skin discolouration:**

- Extravasation of any IV iron preparation can cause pain, inflammation, tissue necrosis and permanent brown skin discoloration.
  - It is important to warn the patient that extravasation of IV iron can lead to permanent skin discoloration.
  - Management:
    - Stop & disconnect infusion (note how much is remaining).
    - Aspirate the cannula with a 10ml syringe and record volume removed (may be none)
    - Remove the canula
    - Mark the affected area
    - Elevate the limb. Avoid pressure at site of extravasation
    - Administer analgesia as required
    - Inform medical team (For injuries involving Venofer® [pH 10.5-11.1] application of a cold pack is advised and plastics team referral should be considered)
    - Provide extravasation leaflet to the patient. Explain that intravenous iron may cause permanent discoloration of the skin at the site of extravasation.
  - If the patient consents, the rest of the infusion can be given via a different cannula/line
- See full [extravasation guideline](#) including specific advice about when to seek advice from a plastic surgeon.

**References:**

- 1 World Health Organisation. Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. (2011).
- 2 Fletcher, A., Forbes, A., Svenson, N. & Wayne Thomas, D. Guideline for the laboratory diagnosis of iron deficiency in adults (excluding pregnancy) and children. *British Journal of Haematology* **196**, 523-529 (2022). <https://doi.org/10.1111/bjh.17900>
- 3 Kotze, A. *et al.* British Committee for Standards in Haematology Guidelines on the Identification and Management of Pre-Operative Anaemia. *Br J Haematol* **171**, 322-331 (2015). <https://doi.org/10.1111/bjh.13623>
- 4 Snook, J. *et al.* British Society of Gastroenterology guidelines for the management of iron deficiency anaemia in adults. *Gut* **70**, 2030-2051 (2021). <https://doi.org/10.1136/gutjnl-2021-325210>
- 5 National Institute for Health and Care Excellence. *Anaemia - iron deficiency*, <<https://cks.nice.org.uk/topics/anaemia-iron-deficiency/prescribing-information/drug-interactions/>> (2023).
- 6 Medicines and Healthcare products Regulatory Agency. *Ferric carboxymaltose (Ferinject): risk of symptomatic hypophosphataemia leading to osteomalacia and fractures*, <<https://www.gov.uk/drug-safety-update/ferric-carboxymaltose-ferinject-risk-of-symptomatic-hypophosphataemia-leading-to-osteomalacia-and-fractures>> (2020).
- 7 Pavord, S. *et al.* UK guidelines on the management of iron deficiency in pregnancy. *Br J Haematol* **188**, 819-830 (2020). <https://doi.org/10.1111/bjh.16221>

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## Appendix: Specialty Specific Guidelines

Specialty	Patient group	Guideline
Cardiology (Heart Failure)	Symptomatic with left ventricular ejection fraction (LVEF) less than 50%, with TSAT less than 20% and Hb less than or equal to 150.  Can also be considered if LVEF greater than or equal to 50% with TSAT less than 20%.	Local: None  National/International: <a href="#">European Society of Cardiology</a>  <a href="#">2023 Focused Update of the 2021 ESC Guidelines for Heart Failure</a>  <b>1<sup>st</sup> line: IV iron</b>
Renal (Chronic kidney disease)	<u>Non-HD (use Ferinject):</u> <ul style="list-style-type: none"> <li>Ferritin less than 100mcg/L (not on ESA) or less than 200mcg/L (on ESA)</li> <li>TSAT less than 20%</li> <li>Ret-He less than 29</li> </ul> <u>HD (use Diafer or Venofer 200 mg every 2 weeks):</u> <ul style="list-style-type: none"> <li>Aim for Ferritin 200-700mcg/L</li> </ul> Other tests are not routinely done	Local: <ul style="list-style-type: none"> <li><a href="#">Intravenous iron for the treatment of renal anaemia in CKD non-HD patients</a></li> <li><a href="#">Intravenous Iron in Haemodialysis</a></li> <li><a href="#">Management of Intravenous Iron in Home HD Patients</a></li> </ul> <b>1<sup>st</sup> line: IV iron</b>
Critical Care	Can be used as part of a strategy for total transfusion avoidance (i.e. patients who refuse RBC transfusion)  Ferritin usually not helpful to diagnose iron deficiency.	Local: None  National/International: <a href="#">European Society of Intensive Care Medicine</a>
GI	Inflammatory bowel disease: <b>IV iron is 1<sup>st</sup> line</b> , particularly in active disease.  Other patient group: <b>Oral iron is 1<sup>st</sup> line</b>	Local: None  National/International: <a href="#">British Gastroenterology Society</a>
Maternity	Symptoms: lethargy, lactation failure, postpartum depression.  May also have implications for neonatal iron stores.  Target haemoglobin <sup>7</sup> : <ul style="list-style-type: none"> <li>Pregnant: Hb less than 110g/L</li> <li>Postpartum: less than 100g/L</li> </ul>	Local: <a href="#">Available here</a>  NB: IV iron is contra-indicated in the first trimester.
Oncology	Regardless of haemoglobin, at least one of: <ul style="list-style-type: none"> <li>Ferritin less than 100 mcg/L</li> <li>Transferrin saturation less than 20%</li> </ul>	Local: <a href="#">Available Here</a>  <b>1<sup>st</sup> line: IV iron</b>
Peri-operative		Local: <a href="#">Available here</a>
GI Surgery	Surgery to stomach or small bowel (Patients at higher risk of oral iron failure due to malabsorption)	<b>1<sup>st</sup> line: Oral iron</b> Assess vitamin B12/folate.
Patients declining RBC transfusion	e.g. Jehovah's Witnesses  Can be used as part of a total transfusion avoidance strategy.	Local: <a href="#">Available here</a>  (NB: does not specifically mention IV iron).