Supplementary Annexure 1: Indications and contraindications for iron infusion.

**Indications for infusion**

- Malabsorption (e.g., coeliac disease, inflammatory bowel disease, weight loss surgery, bowel resection).
- Inadequate diet (e.g., vegan, vegetarian).
- Excess blood loss (chronic occult bleeding, excess menstrual blood loss, childbirth).
- Increased body demand (pregnancy beyond first trimester, rapid growth).
- Anemia of chronic disease/inflammation (eg, chronic kidney disease, cancers, rheumatoid arthritis, and heart failure), in which functional iron deficiency (FID)\(^*\) can be present.
- Intolerance, poor adherence, or unresponsiveness to oral iron.

*FID implies a state in which there is insufficient iron mobilization for erythropoiesis despite normal or high ferritin concentrations with a low transferrin saturation reflecting inadequate iron availability. Maintaining the ferritin level greater than 100–200μg/L in some chronic conditions such as heart failure, renal failure, is important to improve quality of life and reduce hospitalizations.[2]

**Contraindications for infusion**

- Anemia not caused by iron deficiency.
- Known anaphylaxis to the specific iron product.
- Iron overload conditions (e.g., hemochromatosis, hemosiderosis, thalassemia major).
- High-risk patients with serious comorbidities (e.g., moderate to severe failure of the heart, liver, or respiratory organ). Such individuals could be managed at tertiary facilities.

Supplementary Annexure 2: Adverse effects of iron infusion

- Anaphylactic reactions are rare but can be life threatening if not managed properly. Rate is reported less than 0.1%, and even true anaphylaxis is one in 200,000, if reaction associated with high molecular dextran is excluded.[11,12]

Less severe or minor reactions include:

- Facial flushing, urticaria, arthralgia, myalgia, sensation of stiffness in face or limbs.
- Dizziness, headache, nausea, dysgeusia.
- Injection site reactions (pain, discoloration of skin). Staining usually fades over time, but may be permanent, in which case laser therapy could be considered.
- Delayed symptoms may occur 1–2 days post infusion; chills and fever, headache, arthralgia, myalgia, urticaria/rash, angioneurotic oedema.
- Transient hypophosphatemia may also occur, particularly with ferric carboxymaltose (FCM).
Supplementary Annexure 3: Calculation for iron dosage with Ganzoni formula and simplified method.

**Ganzoni formula**

Total iron deficit/requirement (mg) = \{body weight (kg) \times (target Hb - actual Hb in g/L)\} \times 0.24 + iron depot (500 mg).

*Example of calculation for a patient with an ideal body weight of 60 kg and Hb = 80 g/L, and the target Hb is set to be 150 g/L. The total required iron dose = \{60 \times (150 - 80)\} \times 0.24 + 500 mg = 1508 mg (=1500 mg).*

**Simplified method of calculation for iron dosage**

<table>
<thead>
<tr>
<th>Hb(^g) /L</th>
<th>Bodyweight 35 to &lt; 70 kg</th>
<th>Body weight (\geq ) 70 kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 100 g/L</td>
<td>1500 mg</td>
<td>2000 mg</td>
</tr>
<tr>
<td>(\geq 100) g/L</td>
<td>1000 mg</td>
<td>1500 mg</td>
</tr>
</tbody>
</table>

Hb: Hemoglobin.

Supplementary Annexure 4: Preparation and administration of IV iron.

- The iron ampoules/vials should be stored below 25–30°C and protected from light. Do refrigerate nor freeze.
- Obtain informed consent after discussing the pros and cons of the procedure.
- The ideal solution for dilution is 0.9% isotonic saline, as not all formulations are compatible with dextrose. Dilution amount for drip infusion is 250–500 mL, and 10–20 mL for IV push/bolus.
- Use aseptic technique (as for venepuncture).
- Keep a resuscitation kit (including adrenaline) nearby in case of anaphylactic reaction. Adverse reactions can be minimized with a slower infusion rate, particularly initially. Consider taking 30 min instead of 15 min, and using a drip infusion instead of an IV bolus.
- The injector should be seated in a comfortable position if elected for a slow IV bolus.
- Take appropriate observations during the infusion and also at least 30 min post-infusion.
- To avoid or minimize skin staining, you must prevent extravasation by ensuring IV canula inside the vein at the insertion site by the initial running of saline fluid first; then at the end of the infusion, flushing with 20–50 mL of saline fluid and applying an instant compression pressure with cover. Do not rub or massage over the IV/infusion site.
- Do not attempt for IV iron administration without skill for IV canula insertion and proper setup.

IV= intravenous
Supplementary Annexure 5: Further references for comparisons of the four non-dextran formulations (FCM, FDM, ISC, and FOT).


17. Derman R, Roman E, Modiano MR, Achebe MM, Thomsen LL, Auerbach M. A randomized trial of iron isomaltoside versus iron sucrose in patients with iron deficiency anemia.


FCM: Ferric carboxymaltose; FDM: Ferric derisomaltose; FOT: Ferumoxytol; ISC: Iron sucrose.