

## PARENTERAL IRON THERAPY FOR IRON DEFICIENCY ANAEMIA IN PREGNANCY

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### Prevalence and Definition

Anaemia during pregnancy and the postpartum period is commonly caused by **iron deficiency** (>90% of the cases). It is a significant worldwide issue with severe consequences for both mother and developing fetus if left untreated. According to the WHO survey, **38%** of pregnant women in Malaysia have anaemia. Anaemia is defined by WHO and Centre for Disease Control and Prevention as an Haemoglobin (Hb) level of: **<11.0 g/dL** in pregnant women in the **first and third trimester**, **<10.5 g/dL** in the **second trimester** and **<10 g/dL** during **postpartum**. Iron deficiency anaemia (IDA) is ascertained by the presence of anaemia and **low serum ferritin** level (<12-15 g/L), usually with **low serum transferrin saturation** (<15-16%).

### Role of Parenteral Iron Therapy

Oral iron therapy is used first-line to treat IDA in pregnancy as it is cheap, effective and will correct anaemia in most pregnant women, especially if treatment is started early. However, up to 10% of patients taking oral iron therapy can have significant compliance issues. About a third of women also suffer from significant gastrointestinal upset and side effects which make them intolerant of oral iron. Also, oral iron may not successfully correct anaemia before birth of the baby, especially in the presence of risk factors for IDA like inflammatory bowel disease, multiple pregnancy, a short inter-pregnancy interval, substance misuse, teenage status, grand-multiparity and social deprivation. In such cases, parenteral iron therapy serves as a valuable **second-line** therapy in correcting anaemia and replenishing iron stores. It provides **more rapid Hb correction** and reduces the need for blood transfusions in late pregnancy and peripartum.<sup>2</sup> In PPUKM, two parenteral iron formulations are currently available: iron dextran (Cosmofer®) and iron sucrose (Venofer®).

### Iron Dextran (Cosmofer®) vs Iron Sucrose (Venofer®)

	Iron Dextran (Cosmofer®)	Iron Sucrose (Venofer®)
Elemental iron per ampoule	100mg iron per 2ml ampoule	100mg iron per 5ml ampoule
Dosage (Depending on Hb level)	<p><b>IV (Injection/infusion):</b> 100-200mg iron up to 3 times a week.</p> <p>For rapid delivery of iron to iron store, may be administered as total dose infusion up to 20mg/kg</p> <p><b>IM:</b> up to 100mg iron per injection</p> 	<p><b>IV Injection:</b> Total IV single dose not more than 200mg, up to 3 times in 1 week.</p> <p><b>IV Infusion:</b> Max single tolerated dose 7mg/kg once a week (max 500mg).</p> 
Use in Pregnancy	Both are contraindicated in first trimester. Venofer® has more safety data in second & third trimester.	
Use in Lactation	Infant risk cannot be ruled out., preferable not to use	Infant risk is minimal.

Both iron dextran and iron sucrose are **iron-carbohydrate complexes** which share the same mechanism of action and are equally effective. The major difference between these formulation is the versatility of **iron dextran** which offers an additional route of administration (IM) as well as an option to be administered as a **total dose infusion** up to 20mg/kg. On the other hand, the **largest experience** in the published literature is with **iron sucrose**. Data from the use of iron sucrose in pregnant women in the second and third trimester showed no safety concerns for the mother or newborn. It is also the preferable parenteral iron for use in lactation.

When making decision, prescribers should take into consideration the cost, time needed for different route of administration, number of doses required and medical history of patients.

Table 1: Comparison between iron dextran and iron sucrose

### Dose Calculation

Dosing of parenteral iron depends on total iron deficit of the patient, which is calculated based on body weight, target hemoglobin (Hb) level and current Hb level using Ganzoni formula as shown below.

$$\text{Total iron deficit (mg)} = \text{weight (kg)} \times (\text{target Hb} - \text{actual Hb [g/dL]}) \times 2.4 + 500\text{mg iron for iron stores}$$

In pregnant women, **pre-pregnancy weight** should be used (use IBW if obese). Although 15 g/dL is widely used as target Hb level in patients >35kg, a lower **target of 11-12 g/dL** is often used in obstetrics. (In PPUKM, Hb level in OMS is in g/dL.) British Committee for Standards in Haematology recommends 11 g/dL as the Hb target for IDA in pregnancy.<sup>3</sup> **500mg** is routinely **added for iron store** as IDA will not occur until essentially all iron stores have been depleted. A quick reference table for number of ampoules needed is shown below. Each ampoule of Cosmofer® & Venofer® contains 100mg elemental iron.

	Increase in Hb required (g/dL) = Target Hb minus Actual Hb						
Body wt (kg)	1g/dL	2g/dL	3g/dL	4g/dL	5g/dL	6g/dL	7g/dL
40kg	6	7	8	9	10	11	12
45kg	6	7	8	9	10	11	12
50kg	6	7	9	10	11	12	13
55kg	6	8	9	10	12	13	14
60kg	6	8	9	11	12	14	15
65kg	7	8	10	11	13	14	16
70kg	7	8	10	12	13	15	17
75kg	7	9	10	12	14	16	18
80kg	7	9	11	13	15	17	18
85kg	7	9	11	13	15	17	19
90kg	7	9	11	14	16	18	20

Table 2: Quick Reference for number of ampoules (Cosmofer/Venofer) required

For **total dose infusion** of Cosmofer®, if the determined dose required **exceeds 20mg/kg**, it should be given on **two separate days**. This can be done by giving half of the dose on each day, or by giving up to 20mg/kg in the first infusion and the remainder in the second infusion. The first and second doses should be separated by a one-week interval for every 600mg of iron given. If 600mg of iron is given in the first infusion, the second infusion should be administered after one week. If 1200mg of iron is given in the first infusion, the second infusion should be administered after two weeks, and so forth.<sup>4</sup>

### Risk Minimization of Hypersensitivity Reaction

Hypersensitivity reactions (HSR) to IV iron are **rare** but **potentially life-threatening** if not treated promptly. Nevertheless, the benefits of IV iron outweigh its risks in the treatment of IDA when the oral route is insufficient or poorly tolerated. **Caution** is warranted with **every dose** of IV iron that is given, even if previous administrations have been well tolerated. As a good practice and to standardize protocol, we advocate the administration of **test dose before each intravenous administration** for **both** Venofer® and Cosmofer®. In addition, patients should be **closely monitored** for signs and symptoms of HSR **during infusion** and **for at least 1 hour after the end of infusion**.

All IV iron products are **contraindicated** in patients with **known serious hypersensitivity** to any parenteral iron product and in the **first trimester**. After a mild-moderate previous HSR, the same IV iron preparation should not be used again, and a different preparation should be used only after careful consideration. Special precautions are needed if IV iron is to be given to patients with increased risk of HSR, e.g. patients with history of other drug allergy, severe respiratory or cardiac disease, systemic inflammatory disease like lupus erythematosus.<sup>5</sup>

### References :

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**A publication of Drug Information Centre,  
Pharmacy Department, HCTM, PPUKM**

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