Institution Name: Directorate General of Private Health Establishments

Document Title: Guideline for Management of Iron Deficiency Anemia (IDA) With Parenteral Iron in Adult

Approval Process

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Acronyms

ACE	Angiotensin Converting Enzymes
DGPHE	Directorate General Of Private Health Establishments
Hb	Haemoglobin
IDA	Iron Deficiency Anemia
PHE	Private Health Establishments

Chapter One

Introduction

The DGPHE provides this document as a functional guidance to standardize the management of Iron Deficiency Anemia (IDA) With Parenteral Iron in Adult, in the Private Health Establishments (PHE).

Purpose

1. To ensure that all PHE follow a recognized standardized framework and guideline.
2. To guide health professionals in determining the appropriate formulation and dosage of parenteral iron replacement therapy for adults who have been diagnosed with iron deficiency (ID) and/or iron deficiency anemia (IDA).
3. To ensure the recruitment of proper health professionals in the PHE**.**

Scope

This document is applicable to PHE performing parenteral iron in adult.

Chapter Two

Methods & Procedures of Intravenous therapy

In Oman two preparations of intravenous iron (IV) are approved for use:

1. Ferric carboxymaltose (Ferinject)
2. Iron sucrose

IV Iron Therapy Indications

Intravenous iron infusion may be appropriate in:

1. Iron deficiency anemia where treatment to oral iron replacement has been unsuccessful due to intolerance with oral iron therapy.
2. Iron deficiency anemia where oral iron replacement is not indicated due to malabsorption/gastric surgery.
3. A pre-operative situation to rapidly increase haemoglobin as part of a blood management protocol, particularly to decrease or avoid the use of red cell transfusion.
4. Severe anemia from obstetric hemorrhage

Antenatal Indications

1. Persistent Hb < 9 g/dl despite 4 weeks of oral iron treatment
2. Intolerance to oral iron replacement
3. Haemaglobin <10.5 g/dl at 34 weeks gestation, so rapid replacement of iron stores required
4. Inability to absorb oral iron (e.g. active inflammatory bowel disease)
5. Severe antepartum iron deficient anemia non-responsive (or intolerant) to oral iron replacement

Parental Iron Therapy Contraindication

1. Non-iron deficiency anaemia
2. Iron overload/haemachromatosis or risk of iron overload e.g. sickle cell disease
3. Patients with thalassaemia who are diagnosed with iron deficiency anaemia should be reviewed by a haematologist for appropriate management and treatment**.** Patients with **thalassaemia** or **sickle cell disease** should **NEVER** routinely receive iron therapy either oral or intravenous
4. Previous hypersensitivity to parenteral iron
5. Severe asthma or eczema or atopy
6. Hepatic impairment
7. Active infection
8. Oral iron is not required after IV iron is given if the total iron deficit has been (or will be) replete with IV iron therapy.
9. IV Iron preparation must not be used in the first trimester of pregnancy and in children less than the age of 13.

Precautions:

1. May be more likely in patients with a history of asthma and /or other allergic conditions.
2. Previous adverse reaction to other forms of parenteral iron
3. Liver dysfunction (elevated liver enzymes including lactate dehydrogenase occurs following administration)
4. Do not administer to patients currently receiving IV antibiotics for treatment of acute bacterial infection. IV iron may be considered following cessation of IV antibiotics and is dependent upon the woman's condition.

5. Concomitant administration of angiotensin converting enzymes (ACE) inhibitors may increase the incidence of adverse effects of intravenous iron including erythema, abdominal cramps, nausea, vomiting and hypotension
6. Patients with rheumatoid arthritis and other inflammatory diseases may be at particular risk of delayed reaction including fever and reactivation of joint pain

1-Ferinject® (Ferric Carboxymaltose)

Iron Formulation

Ferinject® is the available formulation of iron (ferric) Carboxymaltose. It contains 50mg of iron per ml, two (2) mL ampoule contains 100 mg of elemental iron and a ten (10) mL ampoule contains 500mg of elemental iron

Prescription

Calculate and complete the required dose(s) as determined by the methods below:

Date	**Ferric Carboxymaltose (Ferinject®): in 100mLs of Sodium chloride 0.9% over 15 to 30 minutes** Maximum dose per infusion is 20mg/kg up to a maximum of 1000mg (use ideal body weight if overweight)	**Start Time**	**Administered by**	**Checked by**
..../...../....	**First dose (**20mg/kg up to a maximum of 1000mg)			
..../...../.... At least 1 week later	**Second dose** (remainder of total body iron deficit (not exceeding 20mg/kg up to 1000mg)given ≥1 week later)			

Medical Officer Signature:_____ **Date: /...../…/…...**
Contact Number:_____

Calculation of the total body iron deficit

1. The cumulative dose of Ferric Carboxymaltose (Ferinject®) for repletion of the **total body iron deficit** is based on patient weight (use ideal body weight if overweight) & haemoglobin (Hb) and must not be exceeded.
2. Many patients will require 2 infusions (at least 1 week apart) to cumulatively replace the total body iron deficit (because there is a maximum dose per infusion that CANNOT be exceeded - see 'Dosage per infusion' below).
3. The total body iron deficit can be approximated using the table below. If the **Hb<7g/dl** use the **Ganzoni Equation** (Appendix 1) to calculate the total body iron deficit more precisely. The first dose can however be guided by the <10g/dl section of the table below (3 infusions at least a week apart may be required).
4. Also calculate the total body iron deficit in **iron deficiency with a normal Hb** as it is less than in the table and generally only requires 1 infusion.

Dosage per infusion

1. Maximum dose of Ferric Carboxymaltose (Ferinject®) per infusion is **20mg/kg to maximum of 1000mg**. Use ideal body weight in overweight patients.
2. **The first dose** of Ferric Carboxymaltose (Ferinject®) is given at 20mg/kg to a maximum of 1000mg.
3. **A second dose** can be given ≥1 week later to replace the remainder of the calculated total body iron deficit (see table below) but not exceeding maximum dose per infusion of 20mg/kg to a maximum of 1000mg.
4. **In patients with ongoing blood loss or requiring surgery** associated with substantial blood loss, 20mg/kg to a maximum of 1000mg can be given for both doses.

Adult Approximate Total Body Iron Deficit & Dosage Per-Infusion Of Ferric Carboxymaltose (Ferinject®)

Hb (g/dl)	*Body weight 35 to <50 kg	*Body weight 50 to <70 kg	*Body weight ≥70 kg
#Hb≥10 g/dl	**Total deficit: 1000 mg** 1st dose: 500 mg 2nd dose: 500 mg	**Total deficit: 1000 mg** 1st dose: 1000 mg 2nd dose: not required	**Total deficit: 1500 mg** 1st dose: 1000 mg 2nd dose: 500 mg
#Hb<10 g/dl	**Total deficit: 1400 mg** 1st dose: 700 mg 2nd dose: 700 mg	**Total deficit: 1500 mg** 1st dose: 1000 mg 2nd dose: 500 mg	**Total deficit: 2000 mg** 1st dose: 1000 mg 2nd dose: 1000 mg

Note:

- **If Hb normal or Hb<7 g/dl,** or when preferred by the prescriber, calculate total body iron deficit more precisely using the Ganzoni formula.
- **Use ideal body weight in overweight/obese patients** (If underweight, use actual body weight).
- A *woman's* ideal body weight (medium frame) will be ≥50kg if her height is ≥157 cm or ≥5'2
- A *man's* ideal body weight (medium frame) will be ≥50kg if his height is ≥152 cm or ≥5'0
- In antenatal, pre pregnancy weight should be used.

Administration

Preparation of the Infusion

Iron infusions must be delivered via a volumetric infusion device, no test dose is required.

Carboxymaltose (Ferinject)®must only be mixed with 0.9% Sodium Chloride as there is the potential for precipitation and/or interaction with other solutions and therapeutic agents.

Assemble Equipment

1. Volumetric infusion pump
2. Intravenous administration set
3. Required ampoules of iron (Ferinject ®)
4. Required volume of Sodium Chloride 0.9%
5. Additive label for the fluid bag
6. Syringe/needles to draw up the iron and add to the fluid bag
7. 70% Isopropyl Alcohol swabs

Add Iron to the Infusion Fluid

1. Perform hand hygiene
2. Using aseptic technique, draw up the prescribed iron volume and add it to the infusion bag.
3. Add the label, which includes the patient's name, the name and quantity of the drug, type and quantity of the fluid bag, time and date of preparation. The label is signed by general practitioner and a registered nurse or two (2) nurses
4. Gently rotate the infusion bag to mix the contents.
5. Spike an IV administration set and prime.
6. Insert the administration set into the volumetric pump.

7. Perform hand hygiene.
8. Flush the intravenous cannula with at least 10ml 0.9% Sodium Chloride to ascertain patency of the cannula immediately prior to connecting the iron infusion.

For stability reasons, dilutions to concentrations less than 2 mg iron/mL are not allowed.

Observations (documented)

1. Temperature, pulse, respirations and blood pressure as per normal observations at baseline and at initial 5 minutes, and at the end of the infusion and at 30 minutes post infusion.
2. Patients may be discharged 30 minutes post infusion if observations are satisfactory.
3. Remove the intravenous cannula prior to discharge.

Adverse Effects

1. If there are any adverse effects, cease the infusion immediately, and contact the medical practitioner on site.
2. If the patient complains of pain cease the infusion immediately, do not disconnect line from pt. contact the medical practitioner on site for assessment and treatment.
3. Hypotension is often dose related and the decision may be made to administer the infusion over a longer period of time.

Mild Reactions

1. Manage hypersensitivity reactions by ceasing the infusion for 10-15 minutes, giving **oral Loratidine 10mg (for itch, rash)**, **IV hydrocortisone 100mg** or **paracetamol 1g orally** (headache or discomfort).
2. Usually the infusion can be recommenced once the symptoms have resolved but it may be appropriate to reduce the rate and/or remaining dose.

If anaphylaxis occurs, it is recommended that affected patients are not exposed to further infusions of Iron Carboxymaltose

Immediate symptoms	Delayed symptoms
Bronchospasm with dyspnoea	Dizziness/syncope
Hypotension with circulatory collapse	Chest and/or back pain
Tachycardia	Chills, fever
Facial flushing, faintness, joint, muscle pain	Urticarial and rash
Vomiting and nausea	Stiffness in face and limbs
Headache	Angioneurotic oedema

Mild Reactions

Tissue Infiltration (extravasation) With Iron

Caution should be exercised to avoid para venous leakage when administering Ferinject. Para venous leakage of Ferinject at the injection site may lead to irritation of the skin and potentially long lasting brown discoloration at the site of injection. In case of Para venous leakage, the administration of Ferinject must be stopped immediately.

The important indicator of the severity of the extravasation is **PAIN.** (No necrosis of the skin has ever been reported).

In the event of the iron infusion infiltrating tissue surrounding the intravenous cannula insertion site:

1. Immediate cease the infusion DO NOT DISCONNECT THE LINE.
2. Contact the medical practitioner on site for assessment and treatment
3. Apply a cold compress. **DO NOT COVER THE SITE WITH BANDAGES**

2- Intravenous Iron Sucrose

Dosage

The total cumulative dose of Venofer® should be calculated using the table below. Venofer® can be given as a maximum of 200mg not more than 3 times per week; doses must be 24 hours apart.

Total cumulative Venofer® dose = number of 100mg ampoules for Hb increase.

Dose includes 500mg to replenish iron stores.

Increase in Hb required (g/dL) ie Target Hb minus Actual Hb								
		1g	**2g**	**3g**	**4g**	**5g**	**6g**	**7g**
Body Weight (kg)	**40**	6	7	8	9	10	11	12
	45	6	7	8	9	10	11	12
	50	6	7	9	10	11	12	13
	55	6	8	9	10	12	13	14
	60	6	8	9	11	13	14	16
	65	7	8	10	11	13	14	16
	70	7	8	10	12	13	15	17
	75	7	9	10	12	14	16	18
	80	7	9	11	13	15	17	18
	85	7	9	11	13	15	17	19
	90	7	9	11	14	16	18	20
	95	7	10	12	14	16	19	21
	100	7	10	12	15	17	19	22

Test Dose

The first infusion of Venofer® must include a test dose; facilities for cardiopulmonary resuscitation should be available).

25mg of Venofer® should be infused over a period of 15 minutes. If no adverse events occur during the test dose, the remainder of the dose should be given at an infusion rate of not more than 50ml in 15 minutes.

Drug to diluent	concentration Test dose	Remainder of first dose
100mg Venofer® in 100mL Sodium Chloride 0.9%	25mg in 25mL over 15 mins. (IV pump set 100mls/hr, VTBI 25mL)	75mg in 75mL to be infused. Max infusion rate 200mL/hr
200mg Venofer® in 100mL Sodium Chloride 0.9%	25mg in 12.5mL over 15 mins. (IV pump set 50mL/hr, VTBI 12.5mL)	175mg in 75mL to be infused. Max infusion rate 200mL/hr
200mg Venofer® in 200mL Sodium Chloride 0.9%	25mg in 25mL over 15 mins. (IV pump set 100mL/hr, VTBI 25mL)	175mg in 175mL to be infused. Max infusion rate 200mL/hr

Subsequent Doses

Subsequent doses may be given over 15minutes (100mg) or 30 minutes (200mg).

Administration	
IV infusion	**Rate of administration**
100mg in 100mL Sodium Chloride 0.9%	Administer over at least 15 minutes (maximum pump rate 400mL/hr)
200mg in 100mL or 200mL of Sodium Chloride 0.9%	Administer over at least 30 minutes (maximum pump rate 200mL/hr for 100mL bag, 400mL/hr for 200mL bag)

Example Dosing

72 kg patient; current Hb 8.2g/dL, target Hb 11g/dL - values should be rounded to the nearest whole number as per the dosage chart. ie 70 kg patient Hb 8g/dL **increase required in Hb is 3g/dL.**

Dose required is 10 ampoules i.e. 1g (1000mg).

Administer as:

First dose of 100mg (to include test dose)

Two further doses of 200mg in first week (cumulative total 500mg)

Three doses in second week (two of 200mg and one of 100mg)

NB in obese patients, ideal body weight should be used, in antenatal, pre pregnancy weight should be used.

Adverse Events

Adverse reactions are rare; however facilities for dealing with anaphylaxis and cardiopulmonary resuscitation should be available. It is recommended that the

anaphylaxis box is kept in the close vicinity of a patient receiving IV iron and that administration is carried out by a health care professional.

Adverse drug reactions in clinical trials were; transient taste perversion, hypotension, fever and shivering, injection site reactions and nausea, occurring in 0.5 to 1.5% of patients. Non-serious anaphylactoid reactions occurred rarely

Management of Adverse Events

In the event of a serious anaphylactic or allergic reaction stop the infusion/ IM adrenaline should be administered and appropriate resuscitation measures initiated.

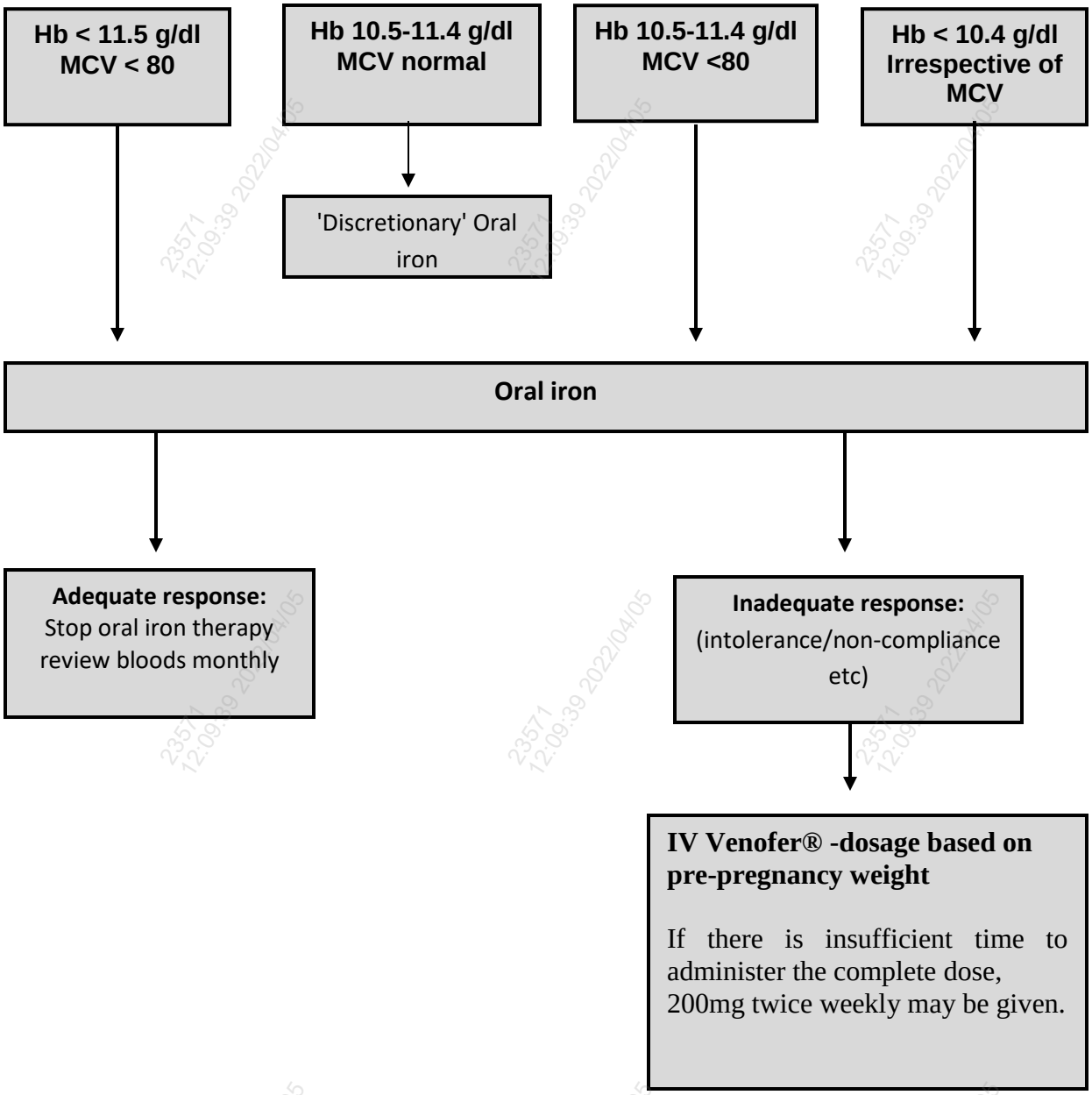
Mild allergic reactions should be managed by stopping the infusion and administering antihistamines.

Hypotensive episodes may occur if administration is too fast, so decrease infusion time as clinically indicated

Treatment of Obstetric Patients with Venofer®

Dosing for antenatal patients should be based on pre-pregnancy weight (or ideal body weight if obese prior to pregnancy). **IV iron must not be used in the 1st trimester of pregnancy. Antenatal treatment (2nd and 3rd trimester only)**

The following flow chart suggests the steps to be followed for anemia in pregnancy. Cases should be assessed on an individual basis with discussion between obstetrician, midwife and patient as appropriate.



Postpartum Treatment

3 doses of 200mg Venofer® administered as IV infusion 24 hours apart. A study of postpartum patients on the above regime (Gravier 1999), with an average haemoglobin of 7.1g/dL, demonstrated a mean increase in haemoglobin of 2.2g/dL by day 7 and 3.9 g/dL by day 14. Non-metabolised iron (III)-hydroxide sucrose complex is unlikely to pass into the mother's milk. Therefore Venofer® should not present a risk to the suckling child.

Follow-up

Full blood count, reticulocyte and iron profile should be checked 3 to 4 weeks after the final dose of Venofer® *where follow up is indicated*.

Chapter Three

Requirements (human resources and their responsibilities)

Prescribing the medication

1- This medication should be prescribed by a senior trained staff (senior specialist/consultant/Sr. Consultant) hematologist or internist or obstetric and gynecologist

2- Whenever possible , parental iron clinic should be established in a private institute with large number of patients requiring IV iron therapy and should be conducted by a qualified hematologist or equivalent as per point 1

3- DGPHE may grant a privilege to qualified physician or obstetric and gynecologist (who do not meet the criteria in point number 1) especially in governorate or willyat with limited or non-available senior staff.

4- Iron infusion may be only delivered if an approval is granted by the PHE to a medical practitioner and a nursing staff (with resuscitation skills) whom should be available throughout the duration of infusion and:

- The procedure should be carried out in a room with emergency equipment
- Utilizing and infusion pump
- The client is not a child

Requesting an Iron Infusion

The doctor requesting the iron infusion is responsible for:

1. Ensuring there are no contraindications for use, discussing the risks and benefits of iron infusion, explaining the procedure and answering any questions
2. Ensuring recent (within 1 month) CBC(complete blood count) and ferritin results are available

3. Prescribing the IV iron on the prescription module
4. Reporting and documentation of any side effects
5. Follow up and monitoring of patient response

References

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Document History and Version Control

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Version	**Description of Amendment**	**Author**	**Review Date**
01	Initial Release	Dr Muhanna Al Muslahi Dr Murtath Al Khabouri Dr Shatha Dr Sulima Al Lamki	March 2022

Appendix: 1. Ganzoni Equation:

The standard method for calculating the total iron deficit is the Ganzoni Equation. This formula gives the total iron deficit and dose in mg for restoration of haemoglobin (Hb) & repletion of body iron stores.

Round the calculated dose to the nearest 100 mg.

Note: vial sizes are 100mg and 500mg.

Total body iron deficit in mg = Iron depot + **[**weight in kg x 0.24 x *(target Hb in g/dl – actual Hb in g/dl)***]**

1. Use ideal body weight if overweight/obese
2. Iron depot (store):

   >34kg weight =500mg

   ≤34kg weight =15mg/kg weight to a maximum of 500mg
3. Target Hb:

   >34kg weight=15g/dl ;

   ≤34kg weight=13 g/dl

Ideal body weight is calculated from the following formula (Australian Medicines Handbook): www.amh.net.au/online/misc/idealweightcalculator.html

1. **Females:** 45.5 kg + 0.9 kg/cm for each cm >152 cm.
2. **Males:** 50 kg + 0.9 kg/cm for each cm >152 cm.

Appendix: 2. Medical Staff Requirement for Haematology

Haematology laboratory	Genetic blood disease, anticoagulation tests, bone marrow sampling, and blood bank	FRCPA or FRCPath Or Omani/British/American/Australian/Canadian Board in Laboratories *clinical certification i.e. FRCP or any of the boards certifications or masters degrees alone does not qualify to work in a laboratory
Haematopathology clinics (benign disease)	Benign blood diseases, genetic blood disease, and blood clotting	FRCPA or FRCPath Senior clinical haematopathologist can treat outpatient and prescribe medications if a letter of permission from the hospital is given proving their management of such cases
Haematopathology clinics (non-benign disease)	Cancerous blood disease	Qualification in internal medicine with fellowship in haematopathology or an approval from the hospital administration granting the right to following up such cases
Haematopathology in-patients	Benign cases	co-supervision of internal medicine doctors and hematolopathologist specialist (can be a visiting dr) or a clinical senior (or above) haematopathologist specialist
	Non-benign cases	a permanent specialized team present, senior (or above) haematopathologist specialist or internal medicine specialist trained in haematopathology, and a nursing team with experience in handling chemo medications and chemo medication prep unite