Guideline for Treatment of Iron Deficiency Anaemia, including Referral to Medical Day Case Unit

University Hospitals of Leicester NHS
NHS Trust

Trust reference
B1/2020

1. Introduction and Who Guideline applies to

- This guideline DOES NOT apply to pregnant women, anaemia in chronic kidney disease and anaemia due to sudden blood loss.
- This guideline aims to provide guidance for the treatment for iron deficiency.
- This guideline applies to primary and secondary care clinicians who wish to refer to Medical Day Case Unit (ward 19 / 17) at LGH for treatment of iron deficiency of iron deficiency anaemia (not for investigations).

2. Guideline Standards and Procedures

- This guideline is presented as a flowchart with additional information and can be found on the following pages.
- This guideline also includes key points and referral pathway to the Leicester General Hospital Day Case Elective Service for Iron Infusion and Blood Transfusion and the standard referral forms (Appendix 1- 4)
- It is the referring doctors responsibility to investigate as felt clinically appropriate and refer to 2WW IDA (Iron Deficiency Anaemia) pathway

Management of Iron Deficiency Anaemia (IDA)

2

Diagnosis

Haemoglobin and MCV

- Men aged over 15 years – Hb <130g/L
- Non-pregnant women aged over 15 years – Hb <120 g/L
- A mean cell volume (MCV) less than 95 femtolitres has a sensitivity of 97.6 % for IDA. Check ferritin level in patients with MCV <95 fl.

Ferritin (UHL reference range : 23 – 540 ug/l)

- Serum ferritin level correlates with total body iron stores and low level indicate low iron stores
- A serum ferritin level of less than 30 micrograms / l confirms the diagnosis of iron deficiency.
- A diagnostic cut-off serum ferritin of 50 micrograms/l indicates iron deficiency in people who have chronic inflammation (CRP > 30 mg/l)

Reticulocyte Hb Content - CHr (UHL reference range: 29 – 34 pg)

- In the absence of Haemoglobinopathies, CHr value less than 29 pg confirms iron deficiency

Once confirmed, establish the cause

Potential Causes (usually multifactorial)

- Dietary deficiency
- Malabsorption (e.g. due to coeliac disease, inflammatory bowel disease, or Helicobacter pylori infection)
- Increased blood loss (e.g. due to chronic blood loss, especially from the uterus or gastrointestinal tract)
- Use of NSAIDs, anti-coagulants or antiplatelet
- Menstruation is the most common cause of IDA in premenopausal women
- Malignancy
- Miscellaneous – blood donation, nosebleeds, haematuria)

- Investigate and treat the cause of anaemia, unless the cause is already known. Seek specialist advice as appropriate (e.g. Gastroenterologist, Gynaecologist, Renal and Haematologist)

Treatment: Oral or IV

Oral indicated if Hb > 80 g/l

IV if Hb < 80 g/l and /or significant symptoms affecting daily activities)

Formulary choice:
Iron isomaltoside (Monofer)

***** Do not wait for investigations to be carried out before prescribing iron supplements *****

Aim

1) To restore haemoglobin level (> 130g/L in men and 120g/L in women) and red cell indices to normal
2) To replenish iron stores

Formulary choice:

□ **Ferrous fumarate 210 mg OD**

□ Swallowing difficulties / enteral drug administration – use oral suspension

□ **Ferrous fumarate liquid 140 mg / 5ml – 280 mg (10 ml) OD**

□ Oral iron can cause significant gastrointestinal side effects that result in poor compliance. A patient who fails to tolerate once preparation may tolerate another (see LMSG (Leicestershire Medicines Strategy Group) for options e.g. ferrous sulphate instead of ferrous fumarate)

□ Treatment should continue for 3 months after iron deficiency is corrected to allow stores to be replenished

If not effective / tolerated, consider treatment with IV

Criteria for IV treatment

- Unable to tolerate two preparations of oral iron
- IBD with significant disease activity (Oral can be used in those with mild IBD disease activity and mild anaemia where intolerance is not a concern)
- Patients who cannot tolerate the gastrointestinal side effects of oral iron
- Not responding to oral treatment
- Malabsorption syndromes (e.g. coeliac disease)
- For surgical patients, when timescale before surgery is limited or rapid iron repletion is clinically important
- Coexisting inflammatory state that interferes with iron homeostasis

Contra-indications for IV treatment

- Delay IV iron administration in patients with active infection until the infection is resolved Decompensated liver disease
- Iron overload or disturbances in utilisation of iron (e.g. haemochromatosis, haemosiderosis)
- Non-iron deficiency anaemia (e.g. haemolytic anaemia
- Known serious hypersensitivity to other parenteral iron products
- Should not be used in patients with hypersensitivity to the active substance, the product itself, or any of its excipients

Iron Isomaltoside (Monofer) administration and dosing

Table 1. Calculating iron need (Simplified Monofer dosage)

Hb (g/L)	Weight <50 kg	Weight 50- 70 kg	Weight > 70 kg
≥100	Refer to dosing in Monofer SPC or contact pharmacy	1000 mg	1500 mg
< 100		1500 mg	2000

NB: units used in SPC are g/dL

Monofer dosing example
Patient weight 60 kg and Hb – 79 g/L. Cumulative iron dose = 1500 mg
Maximum per infusion 20 mg/60 kg = 1200 mg iron
Rx : Day 1 infusion 1200 mg iron
Day 7 + second infusion 300 mg iron

If the cumulative iron dose exceeds 20mg iron / kg body weight, the dose must be split in two administrations with an interval of at least one week.
Give 20 mg iron / kg body weight in the first administration. Depending on clinical judgement, the second administration could wait follow-up laboratory test

Intravenous drip infusion

- Doses up to 1000 mg must be administered over more than 15 minutes.
- Doses exceeding 1000 mg must be administered over 30 minutes or more
- Monofer should be added to maximum 500ml sterile 0.9% sodium chloride

Response to oral therapy

If there is no response to therapy…**RETHINK!**
If Haemoglobin not increasing by 20g/L over approximately three weeks

- Check compliance and duration of treatment
- Consider whether there is evidence of malabsorption, history of gastric resection, inflammatory bowel disease or ongoing gastrointestinal bleeding.
- Consider treatment with intravenous iron therapy

Management of Iron Deficiency Anaemia (IDA)

Monitoring during IV administration

Monitor patients for signs and symptoms of hypersensitivity reactions during and following each administration.
The patient should be observed for adverse effects for at least 30 minutes following each administration.

- Ferritin levels are increased independently of iron status in acute and chronic inflammatory conditions, malignant disease and liver disease. It may be in the normal range despite iron deficiency. In this situation, a CHr (Reticulocyte Hb content) result below the lower limit of the reference range (29 – 34.4 pg) is consistent with iron deficiency in the absence of thalassaemia/haemoglobinopathy.
- It is recommended to consider once daily oral iron dosing to avoid gastrointestinal side effects
- ORAL IRON SHOULD BE STOPPED IF IV IS TO BE ADMINISTERED AND RESTARTED 5 DAYS AFTER FINAL DOSE OF IV IRON.
- It is recommended to use the ideal body weight for obese patients (for both the ganzoni formula in the Monofer SPC and the simplified dosage table in the flow chart above).
- Delay intravenous iron infusions during active infection.
- Response to oral supplementation:
    - Hb concentration will usually begin to rise after approximately one to two weeks of treatment and will rise approximately 20 g/L over the ensuing three weeks. The Hb deficit should be halved by approximately one month, and the Hb level should return to normal by six to eight weeks.
    - Advise GP to monitor FBC every 3 months for 1 year
    - If Hb level and iron stores do not increase with oral therapy check adherence and consider screening for celiac disease and/or Helicobacter pylori infection.
- Response to IV supplementation:
    - Repeat Hb and FBC at least four weeks after final dose. Parenteral iron does not produce a significantly faster haematological response than oral iron.
- Ongoing prophylactic dose of iron (e.g. 210 mg ferrous fumarate tablet daily) may be beneficial in some patients, e.g. Recurring anaemia and further investigations are not indicated or appropriate, Iron-poor diet (for example vegans), malabsorption, menorrhagia, previous gastrectomy
- Blood transfusions should be reserved for patients with or at risk of cardiovascular instability due to the degree of their anaemia.
    - Identification and definitive treatment of the underlying cause must occur simultaneously.
- Exceptional cases
  If there is a history of reaction or intolerance to Monofer then Ferrinject can be used with caution.

Calculating Iron need (Ferinject – Ferric carboxymaltose)

Hb	Patient body weight		
g/L	Below 35 kg	35 to <70 kg	70 kg and above
<100	500 mg	1,500 mg	2,000 mg
100 to <140	500 mg	1,000 mg	1,500 mg
140 and above	500 mg	500	500

- Please refer to the Ferinject SPC for further dosing information or contact pharmacy
- **NB: units used in SPC are g/dL**

3. Education and Training

None

4. Monitoring Compliance

What will be measured to monitor compliance	How will compliance be monitored	Monitoring Lead	Frequency	Reporting arrangements
Incidents reported relating to inappropriate management of anaemia	DATIX reports	ESM Patient Safety team	Annually	ESM Q+S Patient safety reports

5. Supporting References

1) Goddard, A., James, M., McIntyre, A. and Scott, B. (2011). Guidelines for the management of iron deficiency anaemia. Gut, 60(10), pp.1309-1316.
2) Clinical knowledge summaries (2018). Anaemia - iron deficiency. National Institute for Health and Care Excellence. Accessed June 2019 https://cks.nice.org.uk/anaemia-iron-deficiency#!diagnosisSub:2
3) Auerbach, M. (2019). Causes and diagnosis of iron deficiency and iron deficiency anaemia in adults. Uptodate.com. Accessed on June 2019 from https://www.uptodate.com/contents/causes-and-diagnosis-of-iron-deficiency-and-iron-deficiency-anemia-in-adults
4) Summary of Product Characteristics (SPC). Monofer 100mg/ml solution for injection/infusion, Pharmacosmos UK Limited, eMC, Last updated July 2019. Accessed June 2019 https://www.medicines.org.uk/emc/medicine/23669
5) British National Formulary, bnf.org. Last accessed June 2019

6. Key Words

Anaemia, Iron deficiency, Ferrous fumarate, Monofer (iron isomaltoside), Haemoglobin, Intravenous iron

CONTACT AND REVIEW DETAILS	
Dr Cho Phyu – Consultant Physician (Acute medicine) Dr. Amy Webster – Consultant haematologist Dr. James Stewart - Consultant in Gastroenterology, Clinical Nutrition & Intestinal Failure Zainab Mufti – Specialist Medicine Pharmacist David Kearney – CMG Lead Pharmacist Specialist Medicine Rishi Gupta – CMG Lead Pharmacist Emergency Medicine	**Executive Lead** Medical Director

Details of Changes made during review:

1) updated the relevant Hb units to ensure consistence to g/l,
2) formulary choice of oral iron to once daily ferrous fumarate, and
3) Indication for IV iron to ' Hb < 80 g/l and / **OR** significant symptoms affecting daily activities

- All referrals for infusion/transfusion are vetted by a clinician (medical SPR oncall who can have access to medical consultant for support if needed)
- If a referral is from a UHL team / consultant who takes full responsibility on decision and follow-up care, the referral criteria can be a discretionary basic with the agreement from ward 1 SPR and team.

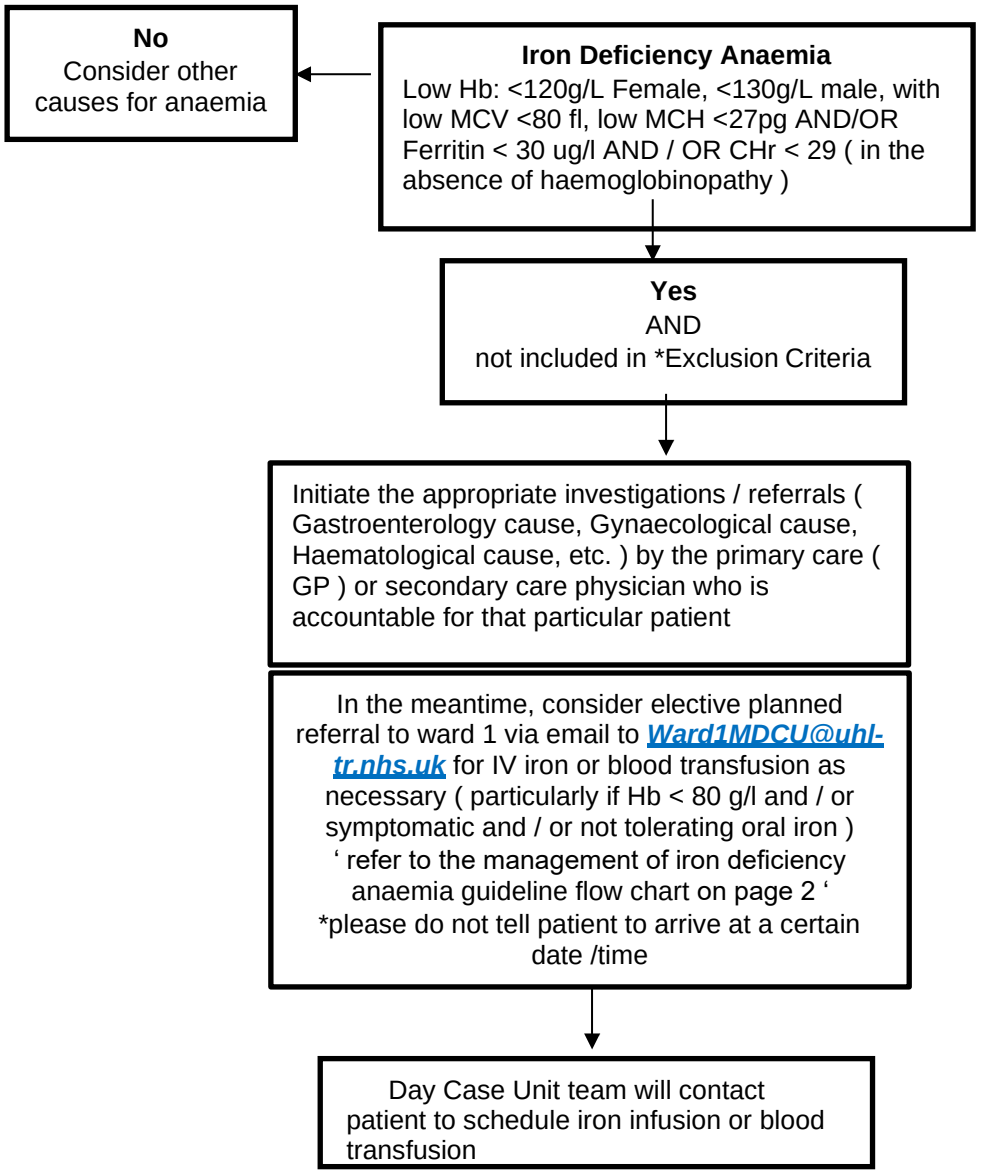
Appendix 1.

Key Points on the Medical Day Case Unit (ward 19 / 17) at Leicester General Hospital for Iron Infusion and Blood Transfusion

- Medical Day Case unit (ward 19/17) at LGH is a daytime service only - there is no provision for overnight stay.
- It is not open over the weekend.
- Medical cover on Medical Day Case Unit (ward 19 / 17) at LGH is only available from the medical registrar on-call for LGH. Very frail patients with multiple co-morbidities should be referred to medicine at the LRI.
- Day Case Unit patients will be explained and given patient information leaflets (when applicable) on Monofer
- All referrals for infusion/transfusion are vetted by a clinician (medical SPR oncall who can have access to medical consultant for support if needed) who reserves the right to decline ward 1 treatment (please refer to the exclusion criteria for the pathway in the flow chart below) but will suggest another service more suitable to that person's needs e.g. GPAU or in-patient treatment.
- If a referral is from a UHL team / consultant who take full responsibility on decision and follow-up care, the referral criteria can be a discretionary basic with the agreement from ward 1 SPR and team.
- Patients with dementia, unless mild and attending with a family member or carer, are unlikely to be suitable for Medical Day Case Unit (ward 19 / 17) at LGH. They must be able to give informed consent for iron infusion or blood transfusion.
- Patients under active follow-up and treatment by oncology or haematology should have their infusions or transfusions organised by those departments rather than referring to ward 1.
- There are patients who fall between services e.g. cancer patients not having treatment or those who have been discharged by oncology, but who suffer with ongoing anaemia – these are suitable for ward 1 if there are no other exclusion criteria.
- The patients will be contacted within 5 working days of referral.
- The responsibility for investigation of the underlying cause of anaemia remains with the referring clinician i.e. GP or referring specialty
- Monitoring response to treatment is also the responsibility of the referring clinician or service

Appendix 2.

Anaemia Referral Pathway to Medical Day Case Unit (ward 19 / 17) at Leicester General Hospital



***Exclusion criteria for this pathway**

- Active bleeding
- Haemodynamic instability
- Acute history of melaena
- Symptomatic with chest pain or short of breath or syncope
- Splenomegaly – if yes refer to haematology
- Immobile patients (unless accompanied by someone)
- Patients with dementia – moderate or severe (unless accompanied by someone)
- Patients on renal replacement therapy
- Oncology or haematology patients under active treatment or follow up

Please note that the monitoring of anaemia in response to the treatment along with ongoing investigations to establish the cause remain the responsibility of the referring clinician

Special circumstances: With the agreed discussion within the team (i.e. ward 1 team including clinician, the referring clinician, the patient and family/carer), the arrangement to attend ward 1 service at the regular interval can be considered. The criteria for special circumstances are those with established underlying cause for anaemia which deemed not for further investigation or active treatment but for regular blood transfusion for symptom control for quality of life. If they require blood transfusion for at least once / month for three consecutive months, they will be discussed within the team to arrange special slot for ward 1 on regular basis.

However, this will be reviewed from time to time. If the circumstances change, there will be another discussion within the team for future ongoing care e.g. more suitable for alternative service, alternative therapy or discontinue the process if the risk outweighs the benefit.

Appendix 3.

INTRAVENOUS IRON REFERRAL FORM (Medical Day Case Unit : ward 19 / 17) – LGH)

Patient Details / ID label	*GP Details*

PATIENT INFORMATION		
	DATE BOOKED	
	DATE ATTENDED	
	Brand / preparation requested **(Circle required product)**	**MONOFER** **FERINJECT (only if previous Monofer allergy)**
	SIMPLIFIED DOSING REGIME	**YES** **NO (state reason why)**
	DATE OF TESTING:	
	PATIENT WEIGHT:	
	HB:	
	FERRITIN:	
	IRON:	
	RETICULOCYTE Hb CONCENTRATION (CHr):	
	ALLERGIES:	

CLINICAL INFORMATION:

NEXT STEP			
	NOTIFY REFERRING CLINICIAN FOLLOWING TREATMENT BY SENDING ICE DISCHARGE LETTER. REFERRER IS RESPONSIBLE FOR FOLLOW UP AND ONGOING MONITORING		
		Further appointment or follow up appointment	

DATE OF REFERRAL: …… REFERRING CLINICIAN ……

NB Referring clinician is responsible for ongoing monitoring

Appendix 4.

Blood transfusion REFERRAL FORM (Medical Day Case Unit : ward 19 / 17) – LGH)

Patient Details / ID label	*GP Details*

PATIENT INFORMATION		**DATE BOOKED FOR TREATMENT – CROSS MATCH/TRANSFUSION**
	Reason for request:	
	PATIENT HISTORY: Cause of blood loss ?active bleeding: Mobility: DNAR: Yes / No (If yes please ensure the patient brings appropriate paperwork)	
	FBC Date of Testing: **HB:** **FERRITIN:** **IRON/TRANSFERRIN SATURATION:** **RETICULOCOUNT HB CONTENT :**	
	ALLERGIES:	

CLINICAL / OTHER INFORMATION:

NEXT STEP			
	NOTIFY REFERRING CLINICIAN FOLLOWING TREATMENT BY SENDING ICE DISCHARGE LETTER. REFERRER IS RESPONSIBLE FOR FOLLOW UP AND ONGOING MONITORING	Further appointment or follow up appointment	

DATE OF REFERRAL: …… REFERRING CLINICIAN ……

NB Referring clinician is responsible for ongoing monitoring