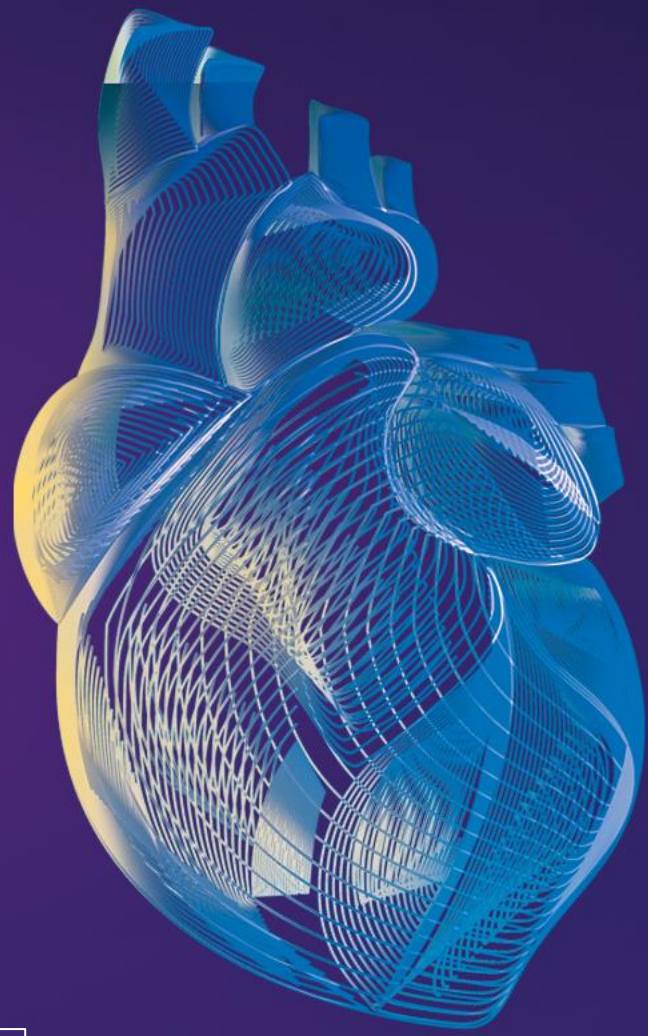
CSL Vifor

HEART AND KIDNEY IN FOCUS

CLINICAL CASES
IRON DEFICIENCY AND ANAEMIA

HEART FAILURE & IRON DEFICIENCY



Prescribing information is available at the end of this chapter, or is available from the location where the booklet is hosted.

Adverse events should be reported.
Reporting forms and information can be found at http://www.hpra.ie/homepage/about-us/report-an-issue.
Adverse events should also be reported to Vifor Pharma UK Ltd Tel: +441276853633 Email: medicalinfo_UK@viforpharma.com.

This promotional booklet was fully funded by Vifor Pharma, including the honoraria for the contributors.
This booklet is intended for healthcare professionals only.

IE-FCM-2300075 | October 2023

HEART FAILURE IS A MAJOR AND GROWING PUBLIC HEALTH PROBLEM

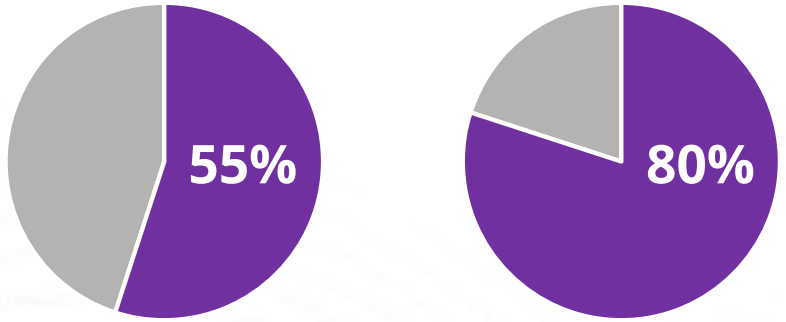
Heart failure inflicts a major burden on patients and the healthcare system

It is estimated that as many as **900,000 people are living with heart failure (HF) in the UK**,[1,2] which represents a burden to the NHS similar to that of all four of the most common cancers combined.[1] Similarly, there are about **90,000 people living with HF in Ireland**.[3]

Patients with HF have poor outcomes, with worse 1-year and 5-year survival rates than those for some common cancers (e.g. prostate cancer and bladder cancer in men, breast cancer in women).[4]
The number of hospitalisations related to HF also increases sharply after the age of 65 years.[5]
In addition to reducing mortality and rehospitalisation, improving quality of life (QoL) for patients with HF is considered a key target for treatment.[6,7]

Iron deficiency is a common modifiable comorbidity in patients with HF

According to the European Society of Cardiology guidelines, multiple studies have shown that iron deficiency, which can be present even in the absence of anaemia, affects up to:[7]



of patients with chronic HF

of patients with acute HF

Figure 1. Iron deficiency affects many patients with HF.[7]

HF, heart failure.

A retrospective study also showed that one in every three adults (33.7%) admitted to hospitals across England with a primary diagnosis of HF also had a documented secondary diagnosis of iron deficiency or iron deficiency anaemia (n=26,530/78,805).[8]

THE PATHOPHYSIOLOGY AND SYMPTOMS OF IRON DEFICIENCY IN HEART FAILURE

Although iron deficiency is associated with several clinical consequences related to erythropoiesis, chronic iron deficiency by itself, independently of anaemia, impairs oxidative metabolism and mitochondrial dysfunction that can cause structural and functional change in the myocardium, leading to cardiac muscle dysfunction.[9,10]

Risk factors for iron deficiency in HF include female sex, more advanced stage of HF, and higher plasma B-type natriuretic peptide (NT-proBNP) and C-reactive protein.[11]

Dysfunctional mitochondrial energy production may contribute to many common symptoms of HF, including:[12]

- progressive worsening of HF state
- deteriorating left ventricular (LV) systolic function and contractility
- impaired LV diastolic function/relaxation
- exercise intolerance
- weakness/fatigue
- insulin resistance
- renal dysfunction/impairment
- poor control of blood pressure.

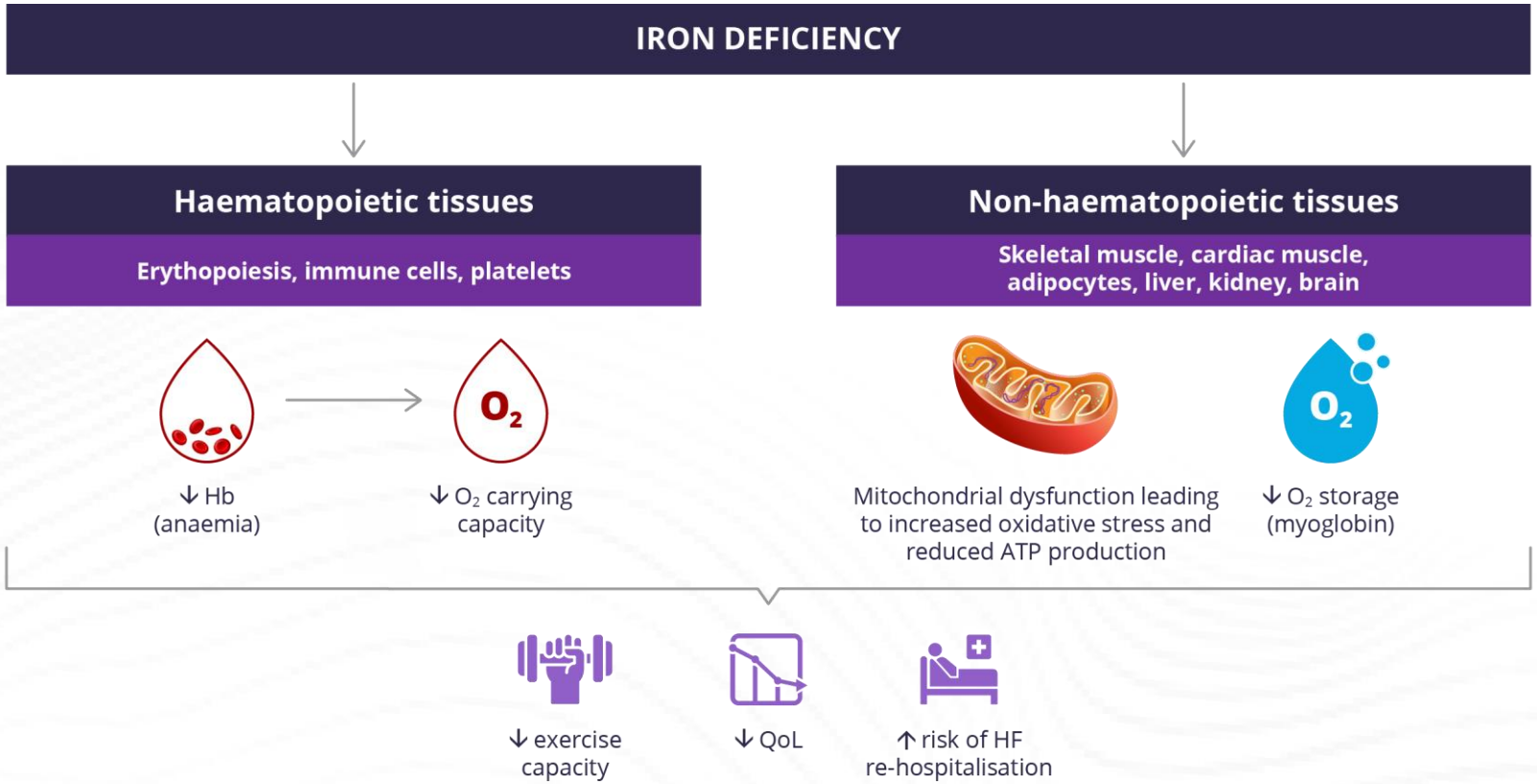


Figure 1. The pathophysiology of adverse outcomes associated with iron deficiency in patients with heart failure. Adapted from Jankowska et al (2013), Cohen-Solal et al (2014) and von Haehling et al (2019).[9–11]

Hb, haemoglobin; HF, heart failure; NYHA, New York Heart Association; O2, oxygen; QoL, quality of life.

CAUSES OF IRON DEFICIENCY

The cause of iron deficiency is multifactorial

The causes of iron deficiency in patients with HF are shown below in **Table 1**.[9,13,14]

Table 1. Causes of iron deficiency in patients with HF.
Adapted from Jankowska et al (2013), Cunha et al (2018) and Cappellini et al (2017).[9,13,14]

Absolute iron deficiency	Functional iron deficiency (iron-restricted erythropoiesis)
• ↓ iron intake (poor nutrition, loss of appetite <50% intake) • ↓ iron absorption due to: – ↓ gastric acidity (e.g. use of PPIs) – gut wall oedema – phosphate binders • ↑ blood loss (e.g. use of anti-platelets, anti-coagulants, NSAIDs, mucosal integrity)	• Inflammation causing ↑ **hepcidin** – ↓ activity of ferroportin – Cytokines IL-6, IL-1β, TNF-α – Hepcidin-mediated malabsorption and iron sequestration

CKD, chronic kidney disease; HF, heart failure; NSAID, non-steroidal anti-inflammatory drug; PPI, proton pump inhibitor; RE, reticuloendothelial.

IDENTIFYING AND DIAGNOSING IRON DEFICIENCY IN HEART FAILURE

Iron deficiency in HF is a strong predictor of poor prognosis

The symptoms suggestive of iron deficiency are **generally vague**, and its diagnosis in HF is often complicated by the **overlapping presence of fatigue and exercise intolerance** in both conditions.[15]

Iron deficiency has been shown to be a **strong independent predictor of poor prognosis**, **reduced exercise capacity** and **impaired health-related QoL** in patients with chronic HF,[16–18] whereas previously it was considered to have clinical consequences only in the presence of anaemia.[19] Additionally, the inclusion of anaemia as an independent predictor of poor prognosis in HF, was indicated to have minor significance.[18]

The 2021 ESC guidelines recommend periodic screening for iron deficiency and anaemia in all patients with HF with a full blood count, serum ferritin concentration and transferrin saturation (TSAT) (Class I recommendation).[7] Table 2 contains the current recommendations for iron deficiency and anaemia thresholds.[7,20,21]

Table 2. Recommended thresholds for iron deficiency and anaemia.

Professional association	Year	HF type	Recommended threshold for anaemia (Hb, g/dL)	Recommended iron deficiency thresholds
European Society of Cardiology (ESC)[7,22]	2021	–	<13 (men); <12 (women)	Serum ferritin <100 ng/mL or ferritin 100-299 ng/mL with TSAT<20%[7,22] Serum ferritin <100 ng/mL or ferritin 100-300 ng/mL with TSAT<20%[20]
Scottish Intercollegiate Guidelines Network (SIGN 147)[20]	2016	HFrEF; NYHA III, LVEF ≤45% or NYHA II, LVEF ≤40%	9.5–13.5	
NICE (NG106)[21]	2018	No thresholds recommended		

Hb, haemoglobin; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; LVEF, left ventricular ejection fraction; NICE, National Institute for Health and Care Excellence; NYHA, New York Heart Association; TSAT, transferrin saturation.

Of note, although the National Institute for Health and Care Excellence's (**NICE**) guideline for chronic HF in adults (NG106) did not recommend any cut-off values for anaemia and iron deficiency,[21] its clinical knowledge summary "Anaemia – iron deficiency" (2021) specifies that when interpreting ferritin level in "chronic kidney disease and other inflammatory conditions, a cut-off of 100 µg/L is advised but needs to be interpreted in addition to other iron studies".[23]

MULTIPLE TRIALS HAVE INVESTIGATED THE EFFICACY AND TOLERABILITY OF IRON DEFICIENCY TREATMENTS IN PATIENTS WITH HF

The efficacy and tolerability of iron supplementation in patients with ID/IDA and HF has been assessed in number of clinical studies (**Figure 2**).

IV iron therapy in patients with HFrEF (LVEF <45%) and ID has been shown to improve QoL, symptoms and exercise capacity.[30]

A recent meta-analysis of seven randomised clinical trials in a total of 2166 patients (1168 in iron therapy and 998 in control) showed a **reduced risk of** the composite outcome of **first HF hospitalisation or cardiovascular mortality** with IV iron therapy, where this outcome was driven primarily by an effect on HF hospitalisations.[38] Results of the recent IRONMAN study were consistent with these findings.[36]

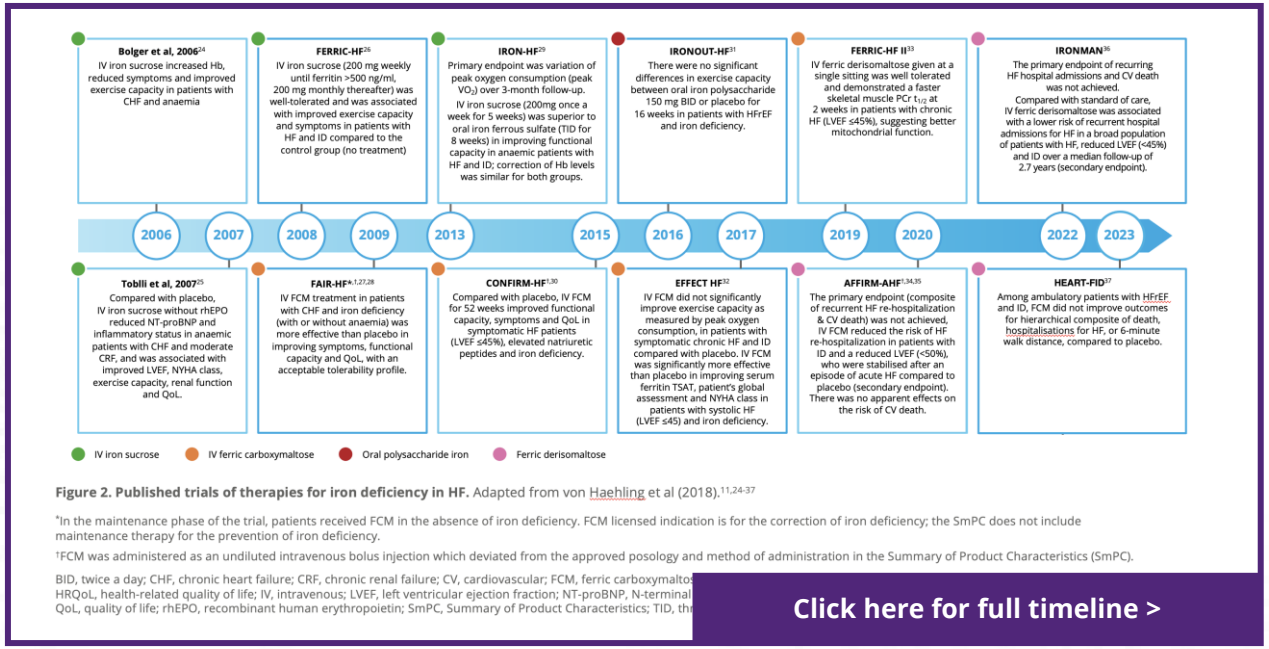


Figure 2. Published trials of therapies for iron deficiency in HF. Adapted from von Haehling et al (2018).[11,24-37]

*In the maintenance phase of the trial, patients received FCM in the absence of iron deficiency. FCM licensed indication is for the correction of iron deficiency; the SmPC does not include maintenance therapy for the prevention of iron deficiency.

†FCM was administered as an undiluted intravenous bolus injection which deviated from the approved posology and method of administration in the Summary of Product Characteristics (SmPC).

BID, twice a day; CHF, chronic heart failure; CRF, chronic renal failure; CV, cardiovascular; FCM, ferric carboxymaltos
HRQoL, health-related quality of life; IV, intravenous; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal
QoL, quality of life; rhEPO, recombinant human erythropoietin; SmPC, Summary of Product Characteristics; TID, thr

Click here for full timeline >

BID, twice a day; CHF, chronic heart failure; CRF, chronic renal failure; CV, cardiovascular; FCM, ferric carboxymaltose; Hb, haemoglobin; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; HRQoL, health-related quality of life; IV, intravenous; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro-brain natriuretic peptide; NYHA, New York Heart Association; PCr, phosphocreatine; QoL, quality of life; rhEPO, recombinant human erythropoietin; SmPC, Summary of Product Characteristics; TID, three times a day; TSAT, transferrin saturation.

RECOMMENDATIONS FOR THE MANAGEMENT OF IRON DEFICIENCY IN HEART FAILURE

Based on clinical trial data, the European Society of Cardiology (ESC) and the Scottish Intercollegiate Guideline Network (SIGN 147) have included a recommendation for treatment of iron deficiency in their guidelines for management of patients with HF (**Table 3**).

Table 3. Guidelines and recommendations for the management of anaemia and iron deficiency in patients with HF.
Adapted from McDonagh et al (2021; focused update 2023), NICE (2018) and SIGN (2016).[7,20-22]

ESC[7,22]	In symptomatic HFrEF and HFmrEF patients with ID:† • IV iron supplementation is recommended to alleviate HF symptoms and improve quality of life (Class I recommendation). • IV FCM or FDM should be considered to reduce the risk of HF hospitalisation (Class IIa recommendation).
SIGN 147[20]	Symptomatic patients with HFrEF and ID:‡ • IV FCM should be considered to improve functional status and QoL.
NICE[21]	At the time of reviewing the clinical evidence, the committee decided that making a recommendation in this area was premature but acknowledged the clinically important benefit of IV iron on QoL for patients with HFrEF.

†Defined by the ESC as serum ferritin <100 µg/L or serum ferritin 100–299 µg/L with TSAT <20% if Hb levels are <13g/dL (men) and <12g/dL (woman).
‡Defined by SIGN 147 as serum ferritin <100 µg/L or <300 µg/L if TSAT <20% if Hb levels are 9.5–13.5g/dL.

ESC, European Society of Cardiology; FCM, ferric carboxymaltose; ; FDM, ferric derisomaltose; HF, heart failure; HFmrEF, heart failure with mildly reduced ejection fraction; HFrEF, heart failure with reduced ejection fraction; ID, iron deficiency; IV, intravenous; LVEF, left ventricular ejection fraction; NICE, National Institute for Health and Care Excellence; QoL, quality of life; SIGN, Scottish Intercollegiate Guidelines Network; TSAT, transferrin saturation.

MULTIPLE ONGOING TRIALS ARE ASSESSING THE EFFICACY AND TOLERABILITY OF IV IRON TREATMENT IN HF

Multiple ongoing trials are investigating the efficacy of oral and IV iron supplementation in patients with HF (**Table 4**).

Table 4. Ongoing trials with IV and oral iron. Adapted from ClinicalTrials.gov records.[37–41]

Trial	Patient population	Treatment arms	Primary endpoint	Completion date
Ongoing trials with IV iron				
FAIR-HFpEF (NCT03074591)	HFpEF and ID (N = 200)	FCM vs placebo	Change in 6MWT distance from baseline to Week 52	July 2021
FAIR-HF2 (NCT03036462)	HFrEF patients (LVEF ≤45%), NYHA Class II or III, with ID (N = 1200)	FCM vs placebo	Combined rate of recurrent hospitalisations for HF and of CV death during follow-up (at least 12 months)	May 2024
Ongoing trials with oral iron				
PREFER-HF (NCT03833336)	HFpEF, IDA (N = 72)	Sucrosomial iron vs ferroglycine sulphate vs FCM vs placebo	Change in 6MWT distance from baseline to Week 24	June 2020
ORION-LVAD-1 (NCT03774615)	HF with LVAD and IDA (N = 25)	Ferric maltol	AEs and SAEs with a relative frequency of at least 11.5%	Terminated (N = 11)

AE, adverse event; CV, cardiovascular; FCM, ferric carboxymaltose; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; ID, iron deficiency; IDA, iron deficiency anaemia; IV, intravenous; LPLV, last patient last visit; LVAD, left ventricular assist device; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; SAE, severe adverse event; 6MWT, 6-minute walk test.

The following case studies have been picked to highlight the points to consider (e.g. identification, diagnosis and treatment initiation) for iron deficiency and anaemia in the management of patients with HF, especially when there is the presence of other comorbidities.

HEART FAILURE & IDA: AN INTRODUCTION – REFERENCES

1. Conrad N et al. Lancet. 2018;391(10120):572–580.
2. British Heart Foundation. UK factsheet. 2023. Available from: https://www.bhf.org.uk/what-we-do/our-research/heart-statistics. Accessed 01 March 2023.
3. Health Service Executive. What is Heart Failure? Available from: https://www.hse.ie/eng/health/hl/living/heartfailure/. Accessed 01 March 2023.
4. Mamas MA et al. Eur J Heart Fail. 2017;19(9):1095–1104.
5. Butrous H and Hummel SL. Can J Cardiol. 2016;32(9):1140–1147.
6. Mizukawa M et al. Int Heart J. 2019;60(6):1293–1302.
7. McDonagh TA et al. Eur J Heart Fail. 2021;42(36):3599–3726.
8. Beattie JM et al. Open Heart. 2020;7(1):e001153.
9. Jankowska EA et al. Eur Heart J. 2013;34(11):816–829.
10. Cohen-Solal A et al. Heart. 2014;100(18):1414–1420.
11. von Haehling S et al. JACC Heart Fail. 2019;7(1):36–46.
12. Brown DA et al. Nat Rev Cardiol. 2017;14(4):238–250.
13. Cunha GJL et al. Eur J Intern Med. 2018;52:1–7.
14. Cappellini MD et al. Am J Hematol. 2017;92:1068–1078.
15. Santhanakrishnan R. US Cardiology Review. 2018;12(2):110–112.
16. Enjuanes C et al. Int J Cardiol. 2014;174(2):268–275.
17. Enjuanes C et al. Rev Esp Cardiol (Engl Ed). 2016;69(3):247–255.
18. Jankowska EA et al. Eur Heart J. 2010;31(15):1872–1880.
19. Zusman O et al. Acta Haematol. 2019;142(1):51–56.
20. SIGN. Management of chronic heart failure [SIGN 147]. 2016. Available from: https://www.sign.ac.uk/assets/sign147.pdf. Accessed 01 March 2023.
21. NICE. Chronic heart failure in adults: diagnosis and management [NG106]. 2018. Available from: https://www.nice.org.uk/guidance/ng106. Accessed 01 March 2023.
22. McDonagh TA et al. Eur Heart J. 2023;ehad195.
23. NICE. What investigations should I arrange to confirm iron deficiency anaemia? 2021. Available from: https://cks.nice.org.uk/topics/anaemia-iron-deficiency/diagnosis/investigations/. Accessed 01 March 2023.
24. Bolger P et al. JACC. 2006;48(6):1225–1227.
25. Toblli JET et al. JACC. 2007;50(17):1657–1665.
26. Okonko DO et al. J Am Coll Cardiol. 2008;51(2):103–112.
27. Anker SD et al. N Engl J Med. 2009;361(25):2436–2448.
28. Comin-Colet J et al. Eur Heart J. 2013;34(1):30–38.
29. Beck-da-Silva L et al. Int J Cardiol. 2013;168(4):3439–3442.
30. Ponikowski P et al. Eur Heart J. 2015;36(11):657–668.
31. Lewis GD et al. JAMA. 2017;317(19):1958–1966.
32. van Veldhuisen DJ et al. Circulation. 2017;136(15):1374–1383.
33. Edwards GC et al. Circulation. 2019;139:2386–2398.
34. Ponikowski P et al. Lancet. 2020;396(10266):1895–1904.
35. Jankowska EA et al. Eur J Heart Fail. 2021;00:1–11.
36. Kalra PR et al. Lancet. 2022: doi: 10.1016/S0140-6736(22)02083-9. [Epub ahead of print]
37. Mentz R et al. N Engl J Med. 2023;389:975–986.
38. Graham FJ et al. Clin Res Cardiol. 2021;110(8):1229–1307.
39. Clinicaltrials.gov. Effect of IV iron in patients with heart failure with preserved ejection fraction (FAIR-HFpEF). Available from: https://clinicaltrials.gov/ct2/show/NCT03074591. Accessed 01 March 2023.
40. ClinicalTrials.gov. Intravenous iron in patients with systolic heart failure and iron deficiency to improve morbidity & mortality (FAIR-HF2). Available from: https://www.clinicaltrials.gov/ct2/show/NCT03036462. Accessed 01 March 2023.
41. Clinicaltrials.gov. Effects of iron therapy in heart failure with preserved ejection fraction and iron deficiency (PREFER-HF). Available from: https://clinicaltrials.gov/ct2/show/NCT03833336. Accessed 01 March 2023.
42. Clinicaltrials.gov. ORal IrON supplementation with ferric maltol in patients with heart failure carrying left ventricular assist devices (ORION-LVAD-1). Available from: https://clinicaltrials.gov/ct2/show/NCT03774615. Accessed 01 March 2023.

Ferinject® (ferric carboxymaltose)

Prescribing Information - Ireland
For full prescribing information refer to the Summary of Product Characteristics (SmPC)
Active Ingredient: Ferric carboxymaltose (50mg/mL)
Presentation: Dispersion for injection/infusion. Available as a 2mL vial (as 100mg of iron), 10mL vial (as 500mg of iron) and 20mL vial (as 1000mg of iron).
Indication: Treatment of iron deficiency when oral iron preparations are ineffective or cannot be used or if there is a clinical need to deliver iron rapidly. The diagnosis must be based on laboratory tests.
Dosage and Administration: The posology of Ferinject follows a stepwise approach:
Step 1: Determination of the iron need:
The individual iron need for repletion using Ferinject is determined based on the patient's body weight and haemoglobin (Hb) level, using the simplified table in the SmPC. Two doses may be required to replenish the total iron need.
Step 2: Calculation and administration of the maximum individual iron dose(s):
Based on the total iron need determined, the appropriate dose(s) of Ferinject should be administered:
In adults and adolescents aged 14 years and older, the maximum single dose is 15 mg iron/kg body weight (for administration by intravenous injection) or 20 mg iron/kg body weight (for administration by intravenous infusion) and the maximum recommended cumulative dose of Ferinject is 1,000 mg of iron (20 mL Ferinject) per week.
In children and adolescents aged 1 to 13 years, the maximum single dose is 15 mg iron/kg body weight, and the maximum recommended cumulative dose of Ferinject is 750 mg of iron (15 mL Ferinject) per week.
In all cases, if the total iron need is higher, then the administration of an additional dose should be a minimum of 7 days apart from the first dose.
Administration rates for intravenous injection using undiluted dispersion:
For iron doses of 100mg to 200mg, there is no prescribed administration time. For doses >200mg to 500mg, Ferinject should be administered at a rate of 100mg iron/min. For doses >500mg to 1,000mg, the minimum administration time is 15 min.
Administration of intravenous drip infusion:
For iron doses of 100mg to 200mg, there is no prescribed administration time. For doses >200mg to 500mg, Ferinject should be administered in a minimum of 6 mins. For doses >500mg to 1,000mg, the minimum administration time is 15 mins.
Ferinject must only be diluted in 0.9% m/V NaCl but should not be diluted to concentrations less than 2 mg iron/mL.
Step 3: Post-iron repletion assessments
Contraindications: Hypersensitivity to Ferinject or any of its excipients. Known serious hypersensitivity to other parenteral iron products. Anaemia not attributed to iron deficiency. Iron overload or disturbances in utilisation of iron.
Special warnings and precautions: Parenterally administered iron preparations can cause potentially fatal anaphylactic reactions. The risk is enhanced for patients with known allergies, a history of severe asthma, eczema or other atopic allergy, and in patients with immune or inflammatory conditions. There have been reports of hypersensitivity reactions which progressed to Kounis syndrome (acute allergic coronary arteriospasm that can result in myocardial infarction). Ferinject should only be administered in the presence of staff trained to manage anaphylactic reactions where full resuscitation facilities are available (including 1:1000 adrenaline solution). Each patient should be observed for 30 minutes following administration. If hypersensitivity reactions or signs of intolerance occur during administration, the treatment must be stopped immediately. Symptomatic hypophosphataemia leading to osteomalacia and fractures requiring clinical intervention has been reported. Patients should be asked to seek medical advice if they experience symptoms. Serum phosphate should be monitored in patients who receive multiple administrations at higher doses or long-term treatment, and those with existing risk factors. In case of persisting hypophosphataemia, treatment with ferric carboxymaltose should be re-evaluated. In patients with liver dysfunction, parenteral iron should only be administered after careful risk/benefit assessment. Careful monitoring of iron status is recommended to avoid iron overload. There is no safety data on the use of single doses of more than 200mg iron in haemodialysis-dependent chronic kidney disease patients. Parenteral iron must be used with caution in case of acute or chronic infection, asthma, eczema or atopic allergies. It is recommended that treatment with Ferinject is stopped in patients with ongoing bacteraemia. In patients with chronic infection a benefit/risk evaluation has to be performed. Caution should be exercised to avoid paravenous leakage when administering Ferinject. The efficacy and safety of Ferinject has not been investigated in children below 1 year of age. Ferinject is therefore not recommended for use in children in this age group.
Special Populations: In adults and adolescents aged 14 years and older, a single maximum daily dose of 200 mg iron should not be exceeded in haemodialysis-dependent chronic kidney disease patients.
In children aged 1 to 13 years with chronic kidney disease requiring haemodialysis, the efficacy and safety of Ferinject has not been investigated. Ferinject is therefore not recommended for use in children aged 1 to 13 years with chronic kidney disease requiring haemodialysis.
A careful risk/benefit evaluation is required before use during pregnancy. Ferinject should not be used during pregnancy unless clearly necessary and should be confined to the second and third trimester. Foetal bradycardia may occur during administration of parenteral irons, as a consequence of hypersensitivity. The unborn baby should be carefully monitored during administration to pregnant women.
Undesirable effects: Common (≥1/100 to <1/10): Hypophosphataemia, headache, dizziness, flushing, hypertension, nausea, injection/infusion site reactions. Rare (≥1/10,000 to <1/1,000): Anaphylactic reactions. Frequency not known: Kounis syndrome, hypophosphataemic osteomalacia. Please consult the SmPC in relation to other undesirable effects
Legal category: POM
MA Number: PA0949/004/001
Date of Authorisation: 19.07.2007
MA Holder: Vifor France, 100-101 Terrasse Boieldieu, Tour Franklin La Défense 8, 92042 Paris La Défense Cedex, France

Ferinject® is a registered trademark

Document number: IE-FCM-2300011
Date of preparation: 06/2023

Additional information is available on request

Adverse events should be reported. Reporting forms and information can be found at: https://www.hpra.ie
Adverse events should also be reported to Vifor Pharma UK Ltd. Tel: +44 1276 853633.
Email: MedicalInfo_UK@viforpharma.com

Venofer® (iron sucrose)

Prescribing Information - Ireland
For full prescribing information refer to the Summary of Product Characteristics (SmPC)
Active ingredient: Iron sucrose (20 mg/mL)
Presentation: Solution for injection/infusion. Available as a 5 mL vial (as 100 mg of iron).
Indication: Treatment of iron deficiency where there is a clinical need for a rapid iron supply, in patients who cannot tolerate oral iron therapy or who are non-compliant, in active inflammatory bowel disease where oral iron preparations are ineffective, and in chronic kidney disease when oral iron preparations are less effective. The diagnosis of iron deficiency must be based on appropriate laboratory tests.
Dosage and Administration: The total cumulative dose of Venofer, equivalent to the total iron deficit (mg), must be individually determined for each patient, based on haemoglobin level and body weight and calculated with the Ganzoni formula. The total single dose must not exceed 200 mg of iron given not more than three times per week.
Administration for intravenous drip infusion:
Venofer must be diluted only in sterile 0.9% m/V sodium chloride solution up to a maximum dilution of 1 mg/mL. For iron doses of 50 mg, minimum infusion time is 8 minutes. For doses of 100 mg, minimum infusion time is 15 minutes. For doses of 200 mg, the minimum administration time is 30 min.
Intravenous injection: Venofer may be administered by slow intravenous injection at a rate of 1 mL undiluted solution per minute and not exceeding 10 mL Venofer (200 mg iron) per injection.
Administration into dialysis machine: Venofer may be administered during a haemodialysis session directly into the venous line of the dialysis machine under the same conditions as for intravenous injection.
Contraindications: Hypersensitivity to Venofer or any of its excipients. Known serious hypersensitivity to other parenteral iron products. Anaemia not attributed to iron deficiency. Iron overload or disturbances in utilisation of iron.
Special warnings and precautions: Parenterally administered iron preparations can cause potentially fatal anaphylactic/anaphylactoid reactions. The risk is enhanced for patients with known allergies, a history of severe asthma, eczema or other atopic allergy, and in patients with immune or inflammatory conditions. There have been reports of hypersensitivity reactions which progressed to Kounis syndrome (acute allergic coronary arteriospasm that can result in myocardial infarction).
Venofer should only be administered in the presence of staff trained to manage anaphylactic reactions where full resuscitation facilities are available (including 1:1000 adrenaline solution). Each patient should be observed for 30 minutes following administration. If hypersensitivity reactions or signs of intolerance occur during administration, the treatment must be stopped immediately. In patients with liver dysfunction, parenteral iron should only be administered after careful risk/benefit assessment. Careful monitoring of iron status is recommended to avoid iron overload. Parenteral iron must be used with caution in case of acute or chronic infection, asthma, eczema or atopic allergies. It is recommended that treatment with Venofer is stopped in patients with ongoing bacteraemia. In patients with chronic infection a benefit/risk evaluation has to be performed. Caution should be exercised to avoid paravenous leakage when administering Venofer.
Special populations: The use of Venofer has not been studied in children. A careful risk/benefit evaluation is required before use during pregnancy. Venofer should not be used during pregnancy unless clearly necessary and should be confined to the second and third trimester. Foetal bradycardia may occur during administration of parenteral irons, as a consequence of hypersensitivity. The unborn baby should be carefully monitored during administration to pregnant women.
Undesirable effects Common (≥1/100 to <1/10): Dysgeusia, hypotension, hypertension, nausea and injection/infusion site reactions. Frequency not known: Anaphylactoid/anaphylactic reactions and Kounis syndrome. Please consult the SmPC in relation to other undesirable effects.
Legal category: POM
MA Number: PA 949/001/002
Date of Authorisation: 11.09.2009
MA Holder: Vifor France, 100-101 Terrasse Boieldieu, Tour Franklin La Défense 8, 92042 Paris La Défense Cedex, France

Venofer® is a registered trademark

Document number: IE-VEN-2200001
Date of preparation: May 2022

Additional information is available on request

Adverse events should be reported. Reporting forms and information can be found at http://www.hpra.ie/homepage/about-us/report-an-issue
Adverse events should also be reported to Vifor Pharma UK Ltd. Tel: +44 1276 853633
Email: medicalinfo_UK@viforpharma.com

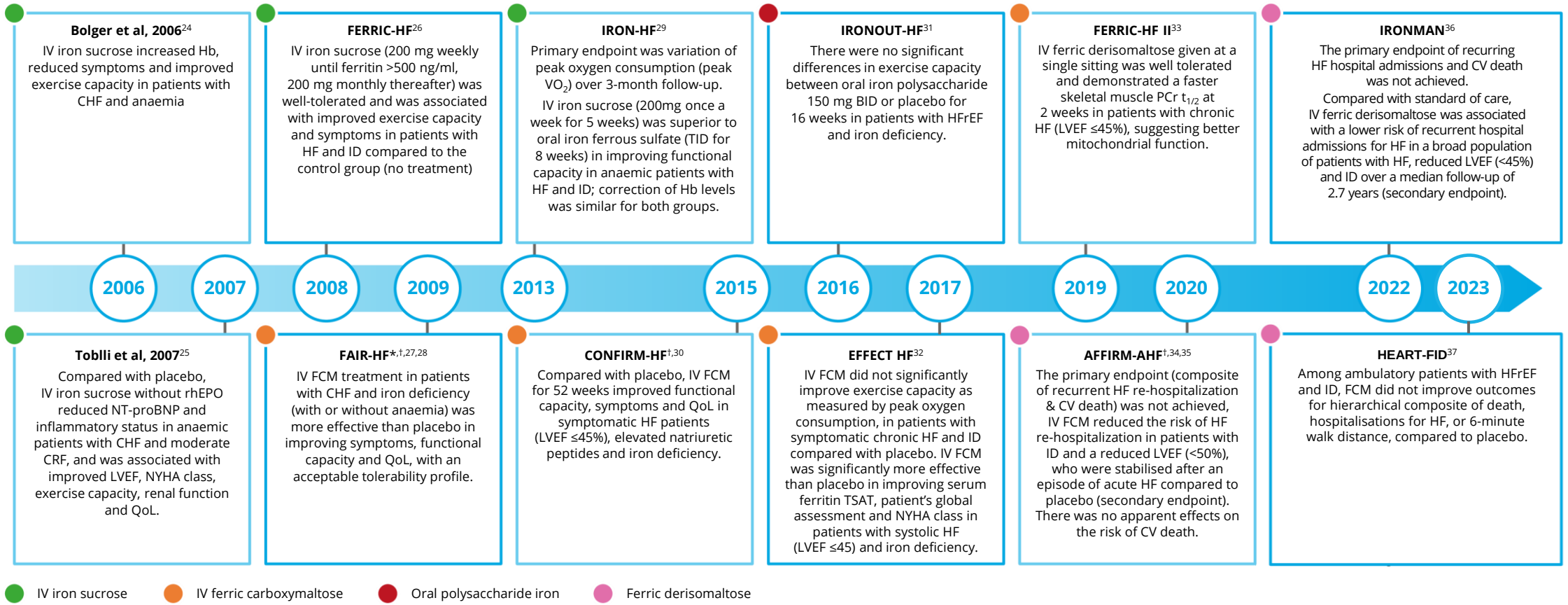


Figure 2. Published trials of therapies for iron deficiency in HF. Adapted from von Haehling et al (2018).[11,24-37]

*In the maintenance phase of the trial, patients received FCM in the absence of iron deficiency. FCM licensed indication is for the correction of iron deficiency; the SmPC does not include maintenance therapy for the prevention of iron deficiency.

†FCM was administered as an undiluted intravenous bolus injection which deviated from the approved posology and method of administration in the Summary of Product Characteristics (SmPC).

BID, twice a day; CHF, chronic heart failure; CRF, chronic renal failure; CV, cardiovascular; FCM, ferric carboxymaltose; Hb, haemoglobin; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; HRQoL, health-related quality of life; IV, intravenous; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro-brain natriuretic peptide; NYHA, New York Heart Association; PCr, phosphocreatine; QoL, quality of life; rhEPO, recombinant human erythropoietin; SmPC, Summary of Product Characteristics; TID, three times a day; TSAT, transferrin saturation.