ferinject®
ferric carboxymaltose

AFFIRM-AHF evaluated the impact of Ferinject® (ferric carboxymaltose) treatment of iron deficiency (ID) on outcomes in patients with heart failure (HF) vs placebo[1]

Ferinject® is indicated for the treatment of iron deficiency when:
- Oral iron preparations are ineffective
- Oral iron preparations cannot be used
- There is a clinical need to deliver iron rapidly

The diagnosis of iron deficiency must be based on laboratory tests.[2]

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

Prescribing information can be found on the last page

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CSL Vifor

AFFIRM-AHF was the first international, multi-centre, double-blind, randomised controlled trial to compare the effect of Ferinject® vs placebo on recurrent hospitalisations and mortality in patients with ID and LVEF <50% stabilised after an episode of acute heart failure (AHF)[1]

Key inclusion criteria

- Iron deficiency (ferritin <100 µg/L, or ferritin between 100-299 µg/L plus transferrin saturation [TSAT] <20%)
- Left ventricular ejection fraction (LVEF) <50%
- Haemoglobin (Hb) 8-15 g/dL

Randomisation 1:1

- Ferinject® n=558
- Placebo n=550

1st dose: shortly before discharge

2nd dose: week 6
(The 1st and 2nd dose was determined based on BW and Hb, as per Ferinject SmPC)

3rd dose: week 12 (500mg only if ID persists)

4th dose: week 24 (500mg only if ID persists)

Study treatment was only administered in subjects for whom Hb ≤ 15 g/dL

Patients treated with Ferinject (ferric carboxymaltose) received an average total dose of 1352 mg, up to the maximum treatment period of 24 weeks[1]

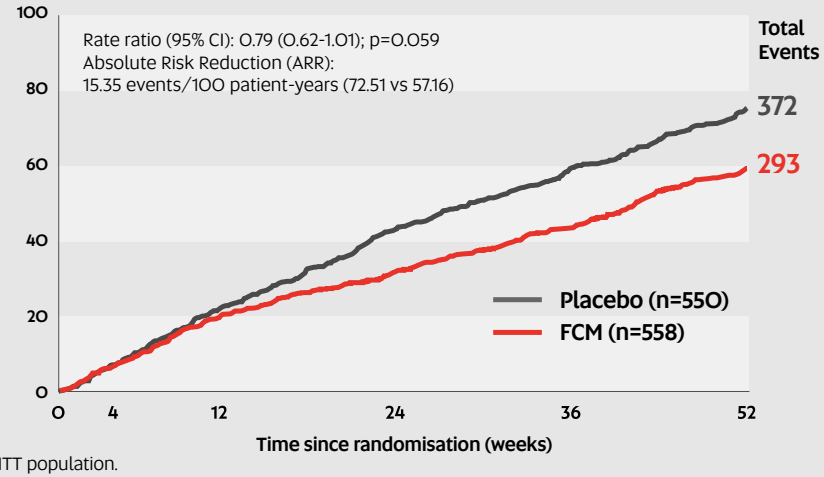
Ferinject® numerically reduced the composite rate of cardiovascular (CV) death and HF re-hospitalisation, but this was not statistically significant[1]

Primary endpoint

The primary endpoint was a composite of total HF hospitalisations and CV death up to 52 weeks of follow-up

The AFFIRM-AHF primary endpoint was not statistically significant (p=0.059)

Total HF Hospitalisations & CV Death



mITT population.

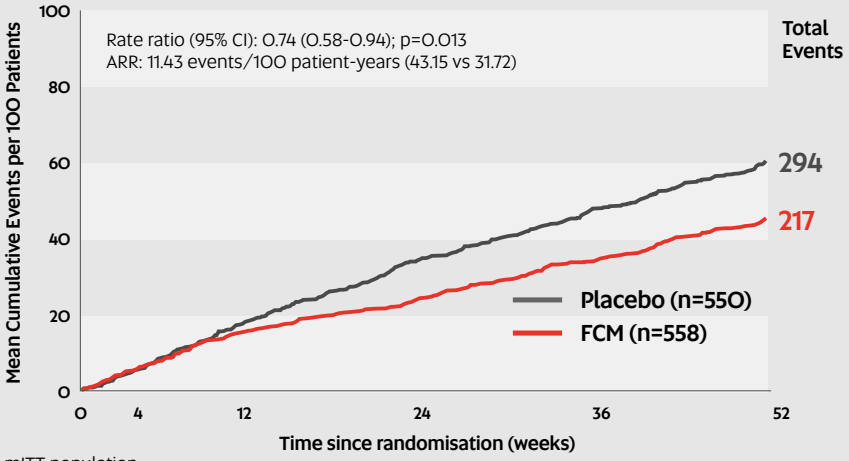
Adapted from Ponikowski et al, 2020.

The effect on the primary endpoint was driven by a 26% reduction in HF re-hospitalisations, with no apparent effect on CV death[1]

Secondary endpoints

Total HF Hospitalisations

Secondary endpoint - component of the primary endpoint (the primary endpoint was not met)



mITT population.

Adapted from Ponikowski et al, 2020.

CV death: component of the primary endpoint: no apparent difference between groups at 14% (77/558) with Ferinject vs 14% (78/550) with placebo (HR [95% CI]: 0.96 [0.70-1.32]; p=0.81. ARR: 0.2 events/100 patient-years (16.1 vs 15.9).

First HF hospitalisation or CV death: occurred in 32% (181/558) of patients assigned Ferinject and in 38% (209/550) patients assigned placebo (HR: [95% CI]: 0.80 [0.66-0.98]; p=0.030. ARR: 9.7 events/100 patient-years).

Days lost due to HF hospitalisations and CV death: reduced by 33% with Ferinject® (369 days/ 100 patient-years with Ferinject compared to 548 days/ 100 patient-years with placebo) (RR: [95% CI]: 0.67, [0.47-0.97]; p=0.035. ARR: 179.4 days/100 patient-years).

AFFIRM-AHF further added to the well-characterised tolerability profile of Ferinject®[1-4]

Overall incidence of adverse events (AEs), serious AEs, and AEs leading to hospitalisation, withdrawal of treatment, or study discontinuation were similar in the Ferinject® and placebo groups[1]

	Ferinject® group (N= 559)*		Placebo group (N=551)*	
	n, (%)	Total events	n, (%)	Total events
Most frequent reported event - Cardiac disorder events	224 (40.1%)	391	244 (44.3%)	453
AEs leading to discontinuation	98 (17.5%)	117	96 (17.4%)	123
Serious adverse events	250 (44.7%)	547	282 (51.2%)	632

*Safety population

Please refer to the Ferinject® Summary of Product Characteristics for complete tolerability information.

ferinject®
ferric carboxymaltose

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

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Additional information is available on request

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Email: medicalinfo_UK@viforpharma.com

References

1. Ponikowski P, et al. Lancet. 2020; 396: 1895-1904 (and supplementary information). **2.** Ferinject® Summary of Product Characteristics. **3.** McDonagh T, et al. Eur J Heart Fail. 2018; 20(12): 1664-1672. **4.** Funk F, et al. Arzneimittelforsch. 2010; 60: 345-353.

AE: adverse event; **AHF:** acute heart failure; **ARR:** absolute risk reduction; **CI:** confidence interval; **COVID-19:** Coronavirus Disease 2019; **CV:** cardiovascular; **ESC:** European Society of Cardiology; **FCM:** ferric carboxymaltose; **Hb:** haemoglobin; **HF:** heart failure; **ID:** iron deficiency; **LVEF:** left ventricular ejection fraction; **mITT:** modified intention-to-treat; **RR:** rate ratio; **TSAT:** transferrin saturation.