NEW ZEALAND DATA SHEET

NAME OF THE MEDICINE

FERINJECT
Ferric carboxymaltose

Chemical structure
The active substance of FERINJECT is a complex of polynuclear iron(III)-hydroxide with 4(R)-(poly-(1→4)-*O*-α-D-glucopyranosyl)-oxy-2(R),3(S),5(R),6-tetrahydroxy-hexanoate.
The relative molecular weight is approximately 150,000 Da, corresponding to the empirical formula:

$[FeO_x(OH)_y(H_2O)_z]_n$ $[\{(C_6H_{10}O_5)_m$ $(C_6H_{12}O_7)\}_l]_k$, where $n \approx 10^3$, $m \approx 8$, $l \approx 11$, and $k \approx 4$.

CAS-Number
1461680-64-7

DESCRIPTION

Solution for intravenous use. FERINJECT is a dark brown, non-transparent, colloidal solution.

Excipients
Sodium hydroxide (for pH adjustment)
Hydrochloric acid (for pH adjustment)
Water for injections

PHARMACOLOGY

Pharmacodynamic properties
Ferric carboxymaltose (FCM) solution for injection/infusion contains iron in a stable ferric state as a complex with a carbohydrate polymer designed to provide iron for the iron transport and storage proteins in the body (transferrin and ferritin). FCM was effective in increasing haemoglobin (Hb) and serum ferritin concentrations in patients with mild to moderate iron-deficiency anaemia. The intravenous (IV) iron dose was 500 mg weekly for up to 4 weeks (n=20) or 1,000 mg weekly for up to 2 weeks (n=26). With the 500 mg iron dose, 37% of patients achieved normal Hb levels within 8 weeks and 75% achieved a ≥20 g/L increase in Hb on at least one occasion. With 1,000 mg iron, 48% of patients achieved normal Hb levels within 6 weeks and 73% achieved a ≥20 g/L increase in Hb on at least one occasion. The target serum ferritin concentration 100-500 µg/L was reached with both doses and remained within the target range at 2 weeks follow-up (at 6 and 4 weeks respectively for the two dose groups)-data were only available for about half the 500 mg iron dose group.

Pharmacokinetic properties
After a single 100 mg IV iron dose of FCM solution (n=6) injected over 1 min, serum iron concentration peaked at a mean of 15 min. After 500, 800 or 1,000 mg iron in 250 mL normal saline infused over 15 min (n=6 for each dose), serum iron concentration peaked at means of 20 min, 1 h and 1.2 h, respectively. The mean volume of distribution was approximately 3 L, corresponding to the plasma volume. Mean plasma clearance ranged from 2.6-4.4 mL/min and terminal half life from 7-12 h. Renal elimination was negligible.

Within 8 h of a single radiolabelled 100 mg IV iron dose of FCM to patients with iron deficiency or renal anaemia, most of the radiolabelled iron had cleared the circulation and distributed to the bone marrow, liver and spleen. Within 6-9 days, the radiolabelled iron was incorporated into the red blood cells. After 24 days, iron utilisation was 91-99% in iron deficiency anaemia and 61-84% in renal anaemia.

CLINICAL TRIALS

Clinical studies showed that the haematological response and the filling of the iron stores was faster after intravenous administration of FCM than with orally administered comparators.

The phase III studies undertaken with FCM included patients with iron deficiency (ID) of different aetiologies, i.e. associated with non-dialysis and dialysis dependent chronic kidney disease (CKD), inflammatory bowel disease, heavy menstrual bleeding, post-partum iron deficiency anaemia (IDA), or patients with chronic heart failure and iron deficiency.

IDA associated with haemodialysis-dependent chronic kidney disease. The efficacy and safety of FCM compared to Venofer® (iron sucrose, intravenous) for the treatment of IDA secondary to chronic renal failure was assessed in a multi-centre, open-label, randomised, parallel-group, Phase III study in 237 patients on haemodialysis or haemodiafiltration. IDA was defined as Hb ≤115 g/L in addition to transferrin saturation (TSAT) <20% and/or serum ferritin <200 µg/L. Patients received 200 mg iron 2 or 3 times weekly (depending on the timing of dialysis sessions) until their individual calculated cumulative dose had been reached. The mean duration of treatment was 15.8 days (range 1 to 27) and 16.2 days (range 1 to 43 days) for the FCM and Venofer® groups, respectively.
Patients treated with erythropoietin (EPO) should have had received this treatment for at least 8 weeks prior to inclusion in the study and increases in the dose of EPO were not permitted. The primary efficacy endpoint was defined as the percentage of patients reaching an increase in Hb of ≥10 g/L at 4 weeks. The percentage of responders was 44.1% (52/118) in the FCM group and 35.3% (41/116) in the Venofer® group; the difference between groups was not statistically significant (chi^2 = 0.2254). At follow-up 4 weeks after the final dose of medication, secondary efficacy parameters (Hb ≥110-120 g/L, serum ferritin 200-800 µg/L, TSAT 20-50%) demonstrated successful increase in iron stores for both treatment groups.

IDA associated with non-dialysis-dependent chronic kidney disease. A multi-centre, randomised, open-label, controlled, 8-week, Phase III study in 255 patients was conducted to compare the safety and efficacy of intravenous infusions of the FCM solution with oral administration of ferrous sulphate, independent of Hb response to EPO,

in treating IDA in non-dialysis-dependent chronic kidney disease (ND-CKD). IDA was defined as Hb ≤110 g/L, TSAT ≤25%, and serum ferritin ≤300 µg/L. Patients treated with EPO should have had received this treatment for at least 8 weeks prior to inclusion in the study and increases in the dose of EPO were not permitted. Patients randomised to FCM treatment received 1 to 3 doses of FCM solution intravenously at 2-4 week intervals: 15 mg iron/kg for weight ≤66 kg to a maximum of 1,000 mg iron for the initial dose and a maximum of 500 mg iron for subsequent doses. Patients randomised to oral iron treatment received ferrous sulphate tablets (65 mg iron) 3 times daily for 8 weeks.

In a modified intent-to-treat analysis which excluded 8 FCM patients and 2 ferrous sulfate patients, the primary efficacy endpoint, defined as the percentage of patients with an increase in Hb ≥10 g/L at any time between baseline and end of study, or time of intervention, was reached by 60.4% (87/144) of FCM-treated patients compared to 34.7% (35/101) of oral iron-treated patients ($p<0.001$; 95% confidence interval (CI) 13.0, 38.5). The modified intent-to-treat population comprised patients with at least one dose of study medication, stable erythropoietin dose, at least one post-baseline Hb assessment and GFR ≤45 mL/min/1.73 m^2. FCM was also demonstrated to be superior to oral iron across all secondary ranked efficacy endpoints: Hb change ≥10 g/L and a serum ferritin change ≥160 µg/L at any time during the study (60.4% versus 0.0%, respectively; $p<0.001$; 95% CI 48.2, 72.6) or a Hb change ≥10 g/L before Day 42 (54.2% versus 28.7%, respectively; $p<0.001$; 95% CI 12.8, 38.1).

In a 44-week extension to this study, the efficacy of FCM in the long-term maintenance treatment of anaemia in ND-CKD was evaluated in 140 patients. Clinical success (Hb ≥110 g/L, serum ferritin 100-800 µg/L, TSAT 30-50%) was achieved in 51.4% (72/140) of patients, with 10% (14/140) exhibiting sustained clinical success at 50% or more of the assessments.

In the ND-CKD subgroup of another study, the safety and efficacy of IV injection of FCM solution, 15 mg iron/kg body weight up to 1,000 mg iron administered over 15 min. was assessed. The comparator was standard medical care (SMC) as determined by the investigator.

The primary endpoint was the incidence of treatment-emergent serious adverse events from Day 0 to 30 days after the last dose of study drug. The safety population contained 204 FCM subjects and 212 SMC subjects. The majority had mild anaemia (mean Hb 104 g/L in FCM group and 102 g/L in control group). There were no serious adverse events assessed as related to FCM. Based on these limited data and the lack of specific serious drug-related adverse reactions, the safety of single FCM doses of 1,000 mg iron appeared equal to SMC.
Efficacy was assessed in a modified intent-to-treat population of 202 FCM subjects and 203 SMC subjects. Achievement of Hb ≥120 g/L was comparable in the two groups at 30 days - FCM 9.9% and SMC 6.9% (Fisher's Exact Test $p = 0.29$).

IDA secondary to inflammatory bowel disease. The efficacy of infusions of FCM solutions compared to oral administration of ferrous sulphate in the treatment of IDA secondary to chronic inflammatory bowel disease was examined in a multi-centre, open-label, randomised, 12-week, Phase III study in 200 patients. 4 patients did not receive study drug and were excluded from the analysis. IDA was defined as Hb ≤110 g/L in combination with TSAT <20% and/or serum ferritin <100 µg/L. Patients were randomised in a 2:1 (FCM: ferrous sulphate) ratio to receive 1 of 2 treatments: FCM intravenous on

Day 1 with subsequent doses at 1-week intervals until the patient's calculated cumulative dose had been reached (a maximum dose of 1,000 mg iron per infusion) or oral ferrous sulphate capsules (100 mg iron) twice daily for 12 weeks. Based on the primary response parameter of change in mean Hb from baseline to Week 12 (36.0 g/L FCM group, 32.9 g/L oral iron group), the results of this study demonstrated that FCM was non-inferior to ferrous sulphate. The non-inferiority criterion was lower limit of 95% CI of difference FCM minus ferrous sulphate ≥–5.0 g/L. The non-inferiority criterion was met in both the intent-to-treat and per protocol populations. Furthermore, the mean Week-12 values of serum ferritin (80.2 µg/L FCM group, 38.6 µg/L oral iron group) and TSAT (23.1% FCM group, 29.2% oral iron group) demonstrated a successful repletion of the iron stores in patients treated with FCM.

In another study, FCM dosing based on a simplified dosing scheme with four Hb-weight subgroups (see Dosage and Administration) was compared with Venofer® dosing based on the Ganzoni formula. The FCM dose was given in up to three IV infusions on Days 1, 8 and 15 in single doses of up to 1000 mg iron. The Venofer® dose was given in up to 11 IV infusions in doses not exceeding 200 mg iron not more than three times per week. The primary endpoint was the percentage of patients achieving a Hb increase ≥20 g/L at Week 12. The demographic and haematological characteristics of the two groups were similar. About 60% of subjects were female, median age was 39 years (range 18-81), median weight 67 kg (range 39-137), median baseline Hb 104 g/L (range 61-146) and median baseline serum ferritin 7 µg/L (range 2-299). Subjects in the two treatment groups achieved at least comparable Hb response overall and in the Hb-weight subgroups (see Table 1).

Table 1. Efficacy of FCM (new dosing method) versus Venofer® (Ganzoni dose calculation) in iron deficiency anaemia associated with inflammatory bowel diseases - trial FER-IBD-07-COR – patients with 12-week assessment

	FCM n=228	**Venofer® n=220**	**Difference [95% CI]**
Hb Response (increase ≥ 20 g/L) at Week 12	65.8%	53.6%	12.2% [3.1%, 21.0%]
	missing n=7	missing n=8	
Hb<100 g/L – Wt 35-<70 kg	**n=59**	**n=44**	
	86.4%	75.0%	11.4% [-4.1%, 26.9%]
Hb<100 g/L – Wt ≥70 kg	**n=31**	**n=24**	
	90.3%	100.0%	-9.7% [-20.1%, 0.7%]
Hb≥100 g/L – Wt 35-<70 kg	**n=70**	**n=78**	
	75.7%	71.8%	3.9% [-10.2%, 18.1%]
Hb≥100 g/L – Wt ≥70 kg	**n=61**	**n=66**	
	88.5%	75.8%	12.8% [-0.3%, 25.8%]

IDA secondary to heavy menstrual bleeding. The safety and efficacy of intravenous infusions of FCM solution, compared to oral administration of ferrous sulphate, in improvement of Hb levels in females with IDA secondary to heavy menstrual bleeding was assessed in a multi-centre, randomised, open-label, 6-week, Phase III study. At enrolment, patients had a baseline Hb ≤114 g/L, TSAT ≤25%, and serum ferritin ≤100 µg/L. Patients were randomised to receive either oral ferrous sulphate tablets (65 mg iron) 3 times daily for 6 weeks or weekly infustions of FCM solution (a

maximum dose of 1,000 mg iron per infusion) until the patient's calculated cumulative dose had been reached, to a maximum of 2,500 mg iron. In a modified intent-to-treat analysis which excluded 18 FCM patients and 6 ferrous sulphate patients, FCM was shown to be superior to oral iron in achieving an increase from baseline in Hb ≥20 g/L at any time during the study: 82.0% (187/228) in the FCM group versus 61.8% (139/225) in the oral iron group (p<0.001; 95% CI 12.2, 28.3). The modified intent-to-treat population comprised patients with at least one dose of study medication, baseline Hb ≤110 g/L, TSAT ≤ 25%, serum ferritin ≤100 µg/L, at least one post-baseline Hb assessment and confirmed diagnosis of heavy menstrual bleeding.

Post partum IDA. The safety and efficacy of FCM compared to oral ferrous sulphate as treatment for post partum IDA (Hb ≤100 g/L or ≤105 g/L) was assessed in 3 randomised, open-label, multi-centre trials. In 2 of the studies, patients were randomised 1:1 to receive either oral ferrous sulphate tablets (65 mg iron) 3 times daily for 6 weeks or weekly intravenous FCM at dosages based on the calculated iron deficit. A maximum of 1,000 mg of iron (15 mg iron/kg body weight for pre-pregnancy weight ≤66 kg), as intravenous FCM solution, was given at weekly intervals until the individual's calculated cumulative iron dose had been reached or a maximum total iron dose of 2,500 mg had been administered. In the third study, patients were randomised 2:1 to receive either oral ferrous sulphate capsules (100 mg iron) twice daily for 12 weeks or weekly intravenous FCM at dosages based on the calculated iron deficit (to a maximum of 3 infusions and not exceeding a weekly dose of 1,000 mg iron).

In all 3 studies, FCM was shown to be efficacious for the treatment of IDA in post partum subjects. In the first study, the superiority of FCM was demonstrated according to the primary efficacy endpoint (defined as Hb >120 g/L), with a greater proportion of patients in the FCM group (91.4%, 127/139) versus the oral iron group (66.7%, 98/147) achieving success at any time during the study (p<0.0001; 95% CI 15.20, 34.20). This was based on a modified intent-to-treat population which excluded 4 FCM patients and one ferrous sulfate patient.

In the second study, FCM was demonstrated to be non-inferior to oral iron among subjects who achieved an increase in Hb ≥20 g/L: 96.4% (162/168) of the FCM group versus 94.1% (159/169) of the oral iron group (95% CI -2.19, 6.88). The analysis was in a modified intent-to-treat population (6 FCM patients and 9 ferrous sulphate patients excluded) and the non-inferiority margin was 15% based on a 1-sided 97.5% CI of the treatment difference. Statistically significantly greater increases from baseline to highest Hb, TSAT, and serum ferritin values were also observed in the FCM groups compared with the oral iron groups.

In the third study, FCM was shown to be non-inferior to ferrous sulphate for the mean change in Hb from baseline to Week 12 (33.4 g/L in the FCM group (n=227) versus 31.8 g/L in the oral iron group (n=117). The non-inferiority criterion was lower limit of 95% CI of difference FCM minus ferrous sulfate ≥–5.0 g/L. The non-inferiority criterion was met in both the intent-to-treat and per protocol populations.

In another study in patients with iron deficiency anaemia due to heavy menstrual bleeding (HMB) or post-partum, the safety and efficacy of IV injection of FCM solution, 15 mg iron/kg body weight up to 1,000 mg iron administered IV over 15 min, was assessed. The comparator was standard medical care (SMC) as determined by the investigator.

The primary endpoint was the incidence of treatment-emergent serious adverse events from Day 0 to 30 days after the last dose of study drug. The safety population contained 996 FCM subjects and 1,022 SMC subjects. Approximately 60% of the subjects had post-partum anaemia (median Hb 103 g/L) and the other 40% anaemia associated with HMB (median Hb 96 g/L). There were no serious adverse events assessed as related to FCM. Based on overall incidences and the lack of specific drug-related serious adverse reactions, the safety profiles of FCM and SMC oral iron appeared similar. There was insufficient exposure to SMC IV iron for it to be included in the assessment.

Efficacy was assessed in a modified intent-to-treat population which was approximately 30% less than the randomised population, although still balanced. Achievement of Hb > 120 g/L was significantly better with FCM than SMC in the two subgroups at 30 days (see Table 2).

Table 2. Efficacy of FCM in single doses up to 1,000 mg iron versus SMC in iron deficiency anaemia associated with heavy menstrual bleeding and post-partum – trial 1VIT07017 – 30 days follow-up - modified intent-to-treat

	FCM	**SMC**	**Difference p-value[2]**
Heavy Menstrual Bleeding	**n=331**	**n=329**	
Hb > 120 g/L[1]	34.4%	15.8%	18.6% p<0.001
Post-Partum	**n=342**	**n=357**	
Hb > 120 g/L[1]	68.1%	50.7%	17.4% p<0.001

FCM: Ferric Carboxymaltose. SMC: Standard Medical Care as determined by the investigator.
[1] Anytime between baseline and end of study of surgical intervention. [2] Fisher's Exact Test.

IDA associated with chronic heart failure and renal deficiency. A pilot study of IV FCM (n=30) versus Venofer® (n=27) and placebo (n=15) in patients with iron deficiency anaemia associated with chronic heart failure and renal deficiency was supportive of improvements in patient global assessment and New York Heart Association (NYHA) status in patients treated with FCM and Venofer®. The study was not powered to show superiority over placebo.

There are no data available regarding the long term use of FERINJECT.

INDICATIONS

FERINJECT is indicated for treatment of iron deficiency when oral iron preparations are ineffective or cannot be used.
The diagnosis must be based on laboratory tests.

CONTRAINDICATIONS

The use of FERINJECT is contraindicated in cases of:

- Hypersensitivity to ferric carboxymaltose complex, to FERINJECT or to any of its excipients
- anaemia not attributed to iron deficiency, e.g. other microcytic anaemia
- evidence of iron overload or disturbances in utilisation of iron

PRECAUTIONS

Iron Overload/Haemosiderosis
Body iron excretion is limited and excess tissue iron can be hazardous causing haemosiderosis. Patients receiving FERINJECT require regular monitoring of red cell indices and serum ferritin to detect iron overload. If there is evidence of iron overload, iron therapy should be withheld.

Patients with Liver Dysfunction
In patients with liver dysfunction, parenteral iron should only be administered after careful risk/benefit assessment. Parenteral iron administration should be avoided in patients with hepatic dysfunction where iron overload is a precipitating factor, in particular Porphyria Cutanea Tarda (PCT).

Patients with Infections
Parenteral iron must be used with caution in case of acute or chronic infection, asthma, eczema or atopic allergies. It is recommended that the administration of FERINJECT is stopped in patients with ongoing bacteraemia. In patients with chronic infection a risk/benefit evaluation has to be performed, taking into account the suppression of erythropoiesis.

Hypersensitivity Reactions
Parenterally administered iron preparations can cause hypersensitivity reactions including anaphylactoid reactions, which may be fatal. Therefore, facilities for cardio-pulmonary resuscitation must be available. If allergic reactions or signs of intolerance occur during administration, the treatment must be stopped immediately.
Hypersensitivity reactions have also been reported after previously uneventful doses of any parenteral iron complexes, including ferric carboxymaltose. Each patient should be observed for adverse effects for at least 30 minutes following each FERINJECT injection.

Paravenous Leakage
Caution should be exercised to avoid paravenous leakage when administering FERINJECT. Paravenous leakage of FERINJECT at the injection site may lead to potentially long lasting brown discolouration and irritation of the skin. In case of paravenous leakage, the administration of FERINJECT must be stopped immediately.

Sodium Content
One mL of undiluted FERINJECT contains up to 5.5 mg (0.24 mmol) of sodium. This should be considered when prescribing FERINJECT to patients on sodium-controlled diets.

Effects on fertility
Reduced weights of reproductive organs (prostate, seminal vesicle, epididymides, testis or uterus) were seen in rats and dogs at maternally toxic doses following repeated IV dosing with ferric carboxymaltose. There were no effects of ferric carboxymaltose on the fertility or reproductive performance of rats given thrice weekly IV doses of up to 30 mg/kg roughly equal to the maximum weekly clinical dose, based on body surface area (BSA).

Use in pregnancy (Category B3)

Studies in rats have shown that iron released from ferric carboxymaltose can cross the placental barrier.

In pregnant and iron-replete rabbits and rats, embryotoxicity (decreased placental or litter weights and increased resorptions) and increases in fetal skeletal abnormalities (thickened/kinked ribs in rats and cranial, forepaw and/or limb abnormalities in rabbits) were observed at maternally toxic IV iron doses from 9 or 30 mg/kg/day, respectively given during organogenesis (1-2 times the maximum weekly clinical dose, based on body surface area (BSA)). No effects were observed at IV iron doses up to 4.5 or 9 mg/kg/day, respectively (0.5 times the maximum weekly clinical dose, based on BSA).

There are no adequate and well-controlled studies in pregnant woman. A careful risk/benefit evaluation is required before use during pregnancy and FERINJECT should not be used during pregnancy unless clearly necessary.

Iron deficiency occurring in the first trimester of pregnancy can in many cases be treated with oral iron. If the benefit of FERINJECT treatment is judged to outweigh the potential risk to the fetus, it is recommended that treatment should be confined to the second and third trimester.

Use in lactation
Clinical studies showed that transfer of iron from FERINJECT to human milk was negligible (≤1%).

Evidence of delayed postnatal growth and development has been observed in rats exposed to ferric carboxymaltose. Milk transfer of administered iron from ferric carboxymaltose was demonstrated in lactating rats. Caution should be exercised when FERINJECT is used in lactating woman.

Paediatric use
The use of FERINJECT has not been studied in children and therefore is not recommended in children under 14 years.

Carcinogenicity
The carcinogenic potential of FERINJECT has not been studied in animals.

Genotoxicity
Ferric carboxymaltose was not genotoxic in assays for gene mutation (in vitro bacterial and mouse lymphoma cell assays) and chromosomal damage (human lymphocytes in vitro and mouse micronucleus test in vivo).

INTERACTIONS WITH OTHER MEDICINES

As with all parenteral iron preparations the absorption of oral iron is reduced when administered concomitantly. Therefore, if required, oral iron therapy should not be started for at least 5 days after the last injection of FERINJECT.

ADVERSE EFFECTS

Clinical studies experience

Adverse drug reactions reported in patients from completed clinical trials are summarized in the table below.

System Organ Class	Very Common (≥1/10)	Common (≥1/100, <1/10)	Uncommon (≥1/1,000, <1/100)	Rare (≥1/10,000, <1/1,000)
Immune System Disorders	–	–	Hypersensitivity	anaphylactoid reactions
Nervous System Disorders	–	Headache, dizziness	Paraesthesia, dysgeusia	–
Cardiac Disorders	–	–	Tachycardia	–
Vascular Disorders	–	Hypertension, flushing	Hypotension	–
Respiratory, Thoracic and Mediastinal Disorders	–	–	Dyspnoea	–
Gastrointestinal Disorders	–	Nausea	Vomiting, dyspepsia, flatulence, abdominal pain, constipation, diarrhoea	–
Skin and Subcutaneous Tissue Disorders	–	–	Pruritus, urticaria, erythema, rash(1)	–
Musculoskeletal and Connective Tissue Disorders	–	–	Myalgia, back pain, arthralgia, pain in extremity, muscle spasms	–
General Disorders and Administration Site Conditions	–	Injection/Infusion site reactions(2)	Pyrexia, fatigue, chest pain, oedema peripheral, pain, chills	Malaise,
Investigations	–	Alanine aminotransferase increased,	Aspartate aminostransferase increased, gamma-glutamyltransferase increased, blood lactate dehydrogenase increased, blood alkaline phosphatase increased	–
Metabolism and Nutritional Disorders	–	Hypophosphataemia	–	–

1 Includes the following preferred terms: rash (individual ADR frequency determined as uncommon) and rash erythematous, -generalised, -macular, -maculo-papular, -pruritic (all individual ADRs are frequency determined as rare).
2 Includes the following preferred terms: injection/infusion site -pain, -haematoma, -discolouration, -extravasation, -irritation, reaction, (all individual ADRs are frequency determined as uncommon) and -paraesthesia (individual ADR frequency determined as rare).
Note: ADR = Adverse drug reaction.

The most commonly reported ADR is headache, occurring in 3.3% of the patients.

Undesirable Effects from Post-marketing Spontaneous Reporting

As part of the continuing post-marketing surveillance of ferric carboxymaltose, the following adverse reactions have been observed:

Post-marketing Spontaneous Reports

System Organ Class	Preferred Terms[(1)]
Nervous System Disorders	Loss of consciousness and vertigo
Psychiatric Disorders	Anxiety
Cardiovascular Disorders	Syncope, Pre-syncope
Skin and Subcutaneous Tissue Disorders	Angioedema, dermatitis, pallor, and face oedema
Respiratory, Thoracic and Mediastinal Disorders	Bronchospasm
General Disorders and Administration Site Conditions	Influenza like illness

1 Frequency not known.

DOSAGE AND ADMINISTRATION

Determination of the cumulative iron dose
The cumulative dose for repletion of iron using FERINJECT is determined based on the patient's body weight and Hb level and must not be exceeded. There are two methods for determining the cumulative dose, the Ganzoni Method and the Simplified Method. Caution is recommended with the Simplified Method since it is based on experience in a single trial in adults with median Hb 104 g/L (range 61-146 g/L) and body weight ≥35 kg – See Clinical Trials.

Patients should be closely monitored when large single doses of FERINJECT (> 200 mg iron) are administered since the safety data are limited.

Post repletion, regular assessments should be done to ensure that iron levels are corrected and maintained.

Ganzoni Method

Cumulative Iron Dose = Body Weight *kg* x (Target Hb – Actual Hb *g/L*) x 0.24 + Iron Stores *mg*

where

Target Hb = 130 g/L for body weight <35 kg and 150 g/L for body weight ≥35 kg

Iron Stores = 15 mg/kg body weight for body weight <35 kg and 500 mg for body weight ≥35 kg.

Round down to nearest 100 mg if body weight ≤66 kg and round up to nearest 100 mg if body weight > 66 kg.

Simplified Method (for patients of body weight ≥ 35 kg)

The cumulative iron dose is determined according to the following table:

Hb g/L	Body weight 35 to < 70 kg	Body weight ≥70 kg
<100	1500 mg	2000 mg
≥100	1000 mg	1500 mg

Intravenous injection:
FERINJECT may be administered by intravenous injection using undiluted solution up to a maximum single dose of 1,000 mg iron (up to a maximum of 20 mg iron/kg body weight). For doses greater than 200 and up to 500 mg iron, FERINJECT should be administered at a rate of 100 mg iron/min. For doses greater than 500 and up to 1,000 mg iron, FERINJECT should be administered over 15 minutes. Do not administer more than 1,000 mg of iron per week.

Intravenous infusion:
FERINJECT may be administered by intravenous infusion up to a maximum single dose of 1,000 mg iron (up to a maximum of 20 mg iron/kg body weight). Do not administer more than 1,000 mg iron per week.

Haemodialysis-dependent chronic kidney disease
In haemodialysis-dependent chronic kidney disease patients, a single daily injection of FERINJECT should not exceed 200 mg iron.

Method of administration
FERINJECT must be administered only by the intravenous route: by bolus injection, or during a haemodialysis session undiluted directly into the venous limb of the dialyser, or by infusion. In case of infusion FERINJECT must be diluted only in sterile 0.9% m/V sodium chloride solution as follows:

Dilution plan of FERINJECT for intravenous infusion

FERINJECT	Iron	Maximum amount of sterile 0.9% m/V sodium chloride solution	Minimum administration time
2 to 4 mL	100 to 200 mg	50 mL	3 minutes
>4 to 10 mL	>200 to 500 mg	100 mL	6 minutes
>10 to 20 mL	>500 to 1,000 mg	250 mL	15 minutes

Note: For stability reasons, dilutions to concentrations less than 2 mg iron/mL (not including the volume of the ferric carboxymaltose solution) are not permissible.

FERINJECT must not be administered by the subcutaneous or intramuscular route.

Inspect vials visually for sediment and damage before use. Use only those containing sediment-free, homogeneous solution.

Each vial of FERINJECT is intended for single use only. Any unused product or waste material should be disposed of in accordance with local requirements.

FERINJECT must only be mixed with sterile 0.9% m/V sodium chloride solution. No other intravenous dilution solutions and therapeutic agents should be used, as there is the potential for precipitation and/or interaction. For dilution instructions, see above.

This medicinal product must not be mixed with other medicinal products than those mentioned above. The compatibility with containers other than polyethylene and glass is not known.

OVERDOSAGE

Administration of FERINJECT in quantities exceeding the amount needed to correct iron deficit at the time of administration may lead to accumulation of iron in storage sites eventually leading to haemosiderosis. Monitoring of iron parameters such as serum ferritin and transferrin saturation may assist in recognising iron accumulation. If iron accumulation has occurred, the use of an iron chelator may be considered.

PRESENTATION AND STORAGE CONDITIONS

Presentations
2 mL of solution in a vial (type I glass) with bromobutyl rubber stopper and aluminium cap in pack sizes of 1 and 5 vials. Each 2 mL vial contains 100 mg of iron as ferric carboxymaltose.

10 mL of solution in a vial (type I glass) with bromobutyl rubber stopper and aluminium cap in pack sizes of 1 and 5 vials. Each 10 mL vial contains 500 mg of iron as ferric carboxymaltose.

Storage conditions
Store in the original package. Do not store above 30 °C. Do not freeze, do not refrigerate.

Shelf-life
Shelf-life of the product as packaged for sale:
36 months.

Shelf-life after first opening of the container:
From a microbiological point of view, preparations for parenteral administration should be used immediately.

Shelf-life after dilution with sterile 0.9% m/V sodium chloride solution:
To reduce microbiological hazard, use as soon as practicable after dilution. If storage is necessary, hold at 2-8°C for not more than 12 hours.

NAME AND ADDRESS OF THE SPONSOR

Pharmacy Retailing
(trading as Healthcare Logistics)
58 Richard Pearce Drive,
Airport Oaks
Managere 2022
New Zealand

CLASSIFICATION

Prescription Medicine

DATE OF PREPARATION

6 June 2016