For the use of a Registered Medical Practitioner or Hospital or a Laboratory only

REDULID FCM

1. Generic Name

Ferric Carboxymaltose Injection

2. Qualitative and Quantitative Composition:

REDULID FCM

Each ml contains:

Ferric Carboxymaltose

Equivalent to elemental Iron…….50 mg

Water for Injections I.P…….q.s.

The Excipients used are Sodium hydroxide solution and hydrochloric acid solution.

3. Dosage form and strength

Dosage form: Injection.

Strength: Ferric Carboxymaltose Injection (100 mg/2 ml)(500 mg/10 ml)(750 mg/15 ml)(1000 mg/20 ml)

4. Clinical particulars

4.1 Therapeutic indication

It is indicated for the treatment of iron deficiency in adults when oral iron preparation are ineffective or cannot be used.

4.2 Posology and method of administration

Posology

Monitor carefully patients for signs and symptoms of hypersensitivity reactions during and following each administration of ferric carboxymaltose.

Ferric Carboxymaltose Injection should only be administered when staff trained to evaluate and manage anaphylactic reactions is immediately available, in an environment where full resuscitation facilities can be assured. The patient should be observed for adverse effects for at least 30 minutes following each Ferric Carboxymaltose Injection.

Calculation of the cumulative iron dose

The cumulative dose for repletion of iron using ferric carboxymaltose is determined based on the patient's body weight and haemoglobin level and must not be exceeded. The following table should be used to determine the cumulative iron dose:

Hb (g/dl)	**Patient Body Weight**		
	Below 35 kg	**35 kg to < 70kg**	**70 kg and over**
< 10	500 mg	1,500 mg	2,000 mg
10 - 14	500 mg	1,000 mg	1,500 mg

> 14	500 mg	500 mg	500 mg

Note: A cumulative iron dose of 500 mg should not be exceeded for patients with body weight <35 kg.

Maximum tolerated single dose

A single Ferric carboxymaltose administration should not exceed:

- 15 mg iron/kg body weight (for administration by intravenous injection) or 20 mg iron/kg body weight (for administration by intravenous infusion)
- 1,000 mg of iron (20 ml Ferric carboxymaltose)

Do not administer 1000 mg of iron (20 ml) more than once a week.

Post-iron repletion assessments

Re-assessment should be performed by the clinician based on the individual patient's condition. The Hb level should be re-assessed no earlier than 4 weeks post final Ferric carboxymaltose administration to allow adequate time for erythropoiesis and iron utilisation.

Special Population - Haemodialysis-dependent chronic kidney disease

A single maximum daily injection dose of 200 mg iron should not be exceeded in haemodialysis dependent chronic kidney disease patients.

Paediatric population

The use of Ferric Carboxymaltose Injection has not been studied in children and therefore is not recommended in children under 14 years.

Method of administration

REDULID FCM must only be administered by the intravenous route:

- By injection, or
- By infusion, or,
- During a haemodialysis session undiluted directly into the venous limb of the dialyser.

Ferric carboxymaltose must not be administered by the subcutaneous or intramuscular route.

Intravenous injection

Ferric carboxymaltose may be administered by intravenous injection using undiluted solution. The maximum single dose is 15 mg iron/kg body weight but should not exceed 1,000 mg iron.

Administration rates for intravenous injection of Ferric Carboxymaltose

Ferric Carboxymaltose	**Equivalent Iron Dose**	**Minimal administration time**
2 to 4 ml	100 to 200 mg	No minimal prescribed time
> 4 to 10 ml	>200 to 500 mg	> 100 mg iron / minute
> 10 to 20 ml	> 500 to 1000 mg	15 minutes

Intravenous infusion

Ferric Carboxymaltose Injection may be administered by intravenous infusion, in which case it must be diluted. The maximum single dose is 20 mg iron/kg body weight, but should not

exceed 1000 mg iron. In case of infusion, Ferric Carboxymaltose Injection must be diluted only in sterile 0.9% sodium chloride solution as follows:

Dilution plan of Ferric Carboxymaltose Injection for intravenous drip infusion

Ferric carboxymaltose	**Equivalent Iron Dose**	**Maximum amount of sterile 0.9% NaCl solution 50 ml 100 ml**	**Minimum administration time**
2 to 4 ml	100 to 200 mg	50 ml	-
> 4 to 10 ml	>200 to 500 mg	100 ml	6 minutes
> 10 to 20 ml	>500 to 1000 mg	250 ml	15 minutes

Note: For stability reasons, dilutions to concentrations less than 2 mg iron/ml are not permissible.

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

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

Ferric Carboxymaltose Injection must only be mixed with sterile 0.9% sodium chloride solution. No other intravenous dilution solutions and therapeutic agents should be used, as there is the potential for precipitation and/or interaction. From a microbiological point of view, preparations for parenteral administration should be used immediately after dilution with sterile 0.9% sodium chloride solution.

4.3 Contraindications

Contraindicated in cases of known hypersensitivity to Ferric Carboxymaltose Injection or to any of its excipients, known serious hypersensitivity to other parenteral iron products, anaemia not attributed to iron deficiency, e.g. other microcytic anaemia, evidence of iron overload or disturbances in utilization of iron and in pregnancy in the first trimester.

4.4 Special warnings and precautions for use

Parenterally administered iron preparations can cause hypersensitivity reactions including anaphylactoid reactions,which may be potentially fatal. Therefore, facilities for cardio-pulmonary resuscitation must be available. Hypersensitivity reactions have also been reported after previously uneventful doses of parenteral iron complexes. The risk is enhanced for patients with known allergies including drug allergies, including patients with a history of severe asthma, eczema or other atopic allergy.

There is also an increased risk of hypersensitivity reactions to parenteral iron complexes in patients with immune or inflammatory conditions (e.g. systemic lupus erythematosus, rheumatoid arthritis).

Ferric Carboxymaltose Injection should only be administered when staff trained to evaluate and manage anaphylactic reactions is immediately available, in an environment where full resuscitation facilities can be assured. Each patient should be observed for adverse effects for

at least 30 minutes following each Ferric Carboxymaltose Injection. If hypersensitivity reactions or signs of intolerance occur during administration, the treatment must be stopped immediately. Facilities for cardio respiratory resuscitation and equipment for handling acute anaphylactic/anaphylactoid reactions should be available, including an injectable 1:1000 adrenaline solution. Additional treatment with antihistamines and/or corticosteroids should be given as appropriate.

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 iş a precipitating factor, in particular Porphyria Cutanea Tarda (PCT). Careful monitoring of iron status is recommended to avoid iron overload. No safety data on haemodialysis-dependent chronic kidney disease patients receiving single doses of more than 200 mg iron are available.

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

Caution should be exercised to avoid paravenous leakage when administering Ferric Carboxymaltose Injection. Paravenous leakage of Ferric Carboxymaltose Injection at the injection site may lead to brown discolouration and irritation of the skin. In case of paravenous leakage, the administration of Ferric Carboxymaltose Injection must be stopped immediately.

The use of Ferric Carboxymaltose Injection has not been studied in children.

As with all parenteral iron preparations the absorption of oral iron is reduced when administered concomitantly.

4.5 Drugs interactions

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 Ferric Carboxymaltose.

4.6 Use in special populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)

Pregnancy

There are no adequate and well-controlled trials of Ferric carboxymaltose in pregnant women. A careful benefit/risk evaluation is required before use during pregnancy and Ferric carboxymaltose should not be used during pregnancy unless clearly necessary. Treatment with Ferric carboxymaltose should be confined to the second and third trimester if the benefit is judged to outweigh the potential risk for both the mother and the foetus. Animal data suggest that iron released from Ferric carboxymaltose can cross the placental barrier and that its use during pregnancy may influence skeletal development in the fetus.

Lactation

Clinical studies showed that transfer of iron from Ferric carboxymaltose to human milk was negligible (<1%). Based on limited data on breast-feeding women it is unlikely that Ferric carboxymaltose represents a risk to the breast-fed child.

4.7 Effects on ability to drive and use machines

Ferric Carboxymaltose Injection is unlikely to impair the ability to drive and use machines.

4.8 Undesirable effects

The most commonly reported ADR is nausea (occurring in 3.1% of the patients), followed by headache, dizziness, and hypertension. Hypophosphataemia (common) may occur. The most serious ADR is anaphylactoid reactions with a frequency of rare.

Reported adverse reactions with ferric carboxymaltose injection are listed below. The following definitions of frequencies are used: common ≥1/100, <1/10; uncommon (≥1/1,000, <1/100) and rare (≥1/10,000, <1/1,000).

Immune system disorders:

Uncommon: Hypersensitivity Rare: anaphylactoid reactions

Nervous system disorders:

Common: Headache, dizziness

Uncommon: Paraesthesia, dysgeusia

Rare: loss of consciousness

Psychiatric disorders:

Rare: Anxiety

Cardiac disorders:

Uncommon: tachycardia

Vascular disorders:

Common: Hypertension, flushing

Uncommon: Hypertension

Rare: Phlebitis, syncope, presyncope

Respiratory, thoracic and mediastinal disorders:

Uncommon: Dyspnoea

Rare: Bronchospasm

Gastrointestinal disorders:

Common: Nausea

Uncommon: Vomiting, dyspepsia, abdominal pain, constipation, diarrhoea Rare: flatulence

Skin and subcutaneous tissue disorders:

Uncommon: Pruritus, urticaria, erythema, rash

Rare: Angioedema, pallor, and face oedema

Musculoskeletal and connective tissue disorders:

Uncommon: Myalgia, back pain, arthralgia, muscle spasm

General disorders and administration site conditions:

Common: Injection site reactions

Uncommon: Pyrexia, fatigue, chest pain, oedema peripheral, chills

Rare: Rigors, malaise, influenza like illness

Investigations:

Uncommon: Alanine aminotransferase increased Aspartate aminotransferase increased, gamma-glutamyltransferase increased, blood lactate dehydrogenase increased, blood alkaline phosphatase increased

Metabolism and nutritional disorders:

Common: Hypophosphataemia

Description of adverse reactions

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at: https://www.torrentpharma.com/index.php/site/info/adverse_event_reporting By reporting side effects, you can help provide more information on the safety of this medicine.

4.9 Overdose

Administration of Ferric Carboxymaltose Injection 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 hemosiderosis. Monitoring of iron parameters such as serum ferritin and transferrin saturation may assist in recognizing iron accumulation. If iron accumulation has occurred, treat according to standard medical practice, e.g. consider the use of an iron chelator.

5 Pharmacological properties

5.1 Mechanism of Action

Ferric carboxymaltose is a colloidal iron (III) hydroxide in complex with carboxymaltose, a carbohydrate polymer that releases iron.

5.2 Pharmacodynamic properties

Pharmacotherapeutic group: Iron trivalent, parenteral preparation, ATC code: B03AC Ferric carboxymaltose injection dispersion for injection/infusion is a colloidal solution of the iron complex ferric carboxymaltose.

The complex is designed to provide, in a controlled way, utilisable iron for the iron transport and storage proteins in the body (transferrin and ferritin, respectively). Red cell utilisation of 59Fe from radio-labelled Ferric carboxymaltose injection ranged from 91% to 99% in subjects with iron deficiency (ID) and 61% to 84% in subjects with renal anaemia at 24 days post-dose.

Ferric carboxymaltose injection treatment results in an increase in reticulocyte count, serum ferritin levels and TSAT levels to within normal ranges.

Clinical efficacy and safety

The efficacy and safety of Ferric carboxymaltose injection has been studied in different therapeutic areas necessitating intravenous iron to correct iron deficiency. The main studies are described in more detail below.

Cardiology

Chronic heart failure

Study CONFIRM-HF was a double-blind, randomised, 2-arm study comparing Ferric carboxymaltose injection (n=150) vs. placebo (n=151) in subjects with chronic heart failure and ID for a treatment period of 52 weeks. At Day 1 and Week 6 (correction phase), subjects received either Ferric carboxymaltose injection according to a simplified dosing grid using

baseline Hb and body weight at screening (see section 4.2), placebo or no dose. At Weeks 12, 24, and 36 (maintenance phase) subjects received Ferric carboxymaltose injection (500 mg iron) or placebo if serum ferritin was <100 ng/mL or 100-300 ng/mL with TSAT <20%. The treatment benefit of Ferric carboxymaltose injection vs. placebo was demonstrated with the primary efficacy endpoint, the change in the 6-minute walk test (6MWT) from baseline to Week 24 (33±11 metres, p=0.002). This effect was sustained throughout the study to Week 52 (36±11 metres, p<0.001).

Study EFFECT-HF was an open-label (with blinded endpoint evaluation), randomised, 2-arm study comparing Ferric carboxymaltose injection (n=86) vs. standard of care (n=86) in subjects with chronic heart failure and ID for a treatment period of 24 weeks. At Day 1 and Week 6 (correction phase), subjects received either Ferric carboxymaltose injection according to a simplified dosing grid using baseline Hb and body weight at screening (see section 4.2) or standard of care. At Week 12, (maintenance phase) subjects received Ferric carboxymaltose injection (500 mg iron) or standard of care if serum ferritin <100 ng/mL or 100 to 300 ng/mL and TSAT <20%. The treatment benefit of Ferric carboxymaltose injection vs. standard of care was demonstrated with the primary efficacy endpoint, the change in weight-adjusted peak VO2 from baseline to Week 24 (LS Mean 1.04 ±0.44 p=0.02).

Nephrology

Haemodialysis-dependent chronic kidney disease

Study VIT-IV-CL-015 was an open-label, randomised parallel group study comparing Ferric carboxymaltose injection (n=97) to iron sucrose (n=86) in subjects with ID anaemia undergoing haemodialysis. Subjects received Ferric carboxymaltose injection or iron sucrose 2-3 times per week in single doses of 200 mg iron directly into the dialyser until the individually calculated cumulative iron dose was reached (mean cumulative dose of iron as Ferric carboxymaltose injection: 1,700 mg). The primary efficacy endpoint was the percentage of subjects reaching an increase in Hb of ≥1.0 g/dL at 4 weeks after baseline. At 4 weeks after baseline, 44.1% responded to treatment with Ferric carboxymaltose injection (i.e. Hb increase of ≥1.0 g/dL) compared to 35.3% for iron sucrose (p=0.2254).

Non-dialysis-dependent chronic kidney disease

Study 1VIT04004 was an open-label, randomised active-control study, evaluating the safety and efficacy of Ferric carboxymaltose injection (n=147) vs. oral iron (n=103). Subjects in the Ferric carboxymaltose injection group received 1,000 mg of iron at baseline and 500 mg of iron at days 14 and 28, if TSAT was <30% and serum ferritin was <500 ng/mL at the respective visit. Subjects in the oral iron arm received 65 mg iron TID as ferrous sulphate from baseline to day 56. Subjects were followed-up until day 56. The primary efficacy endpoint was the percentage of subjects achieving an increase in Hb of ≥1.0 g/dL anytime between baseline and end of study or time of intervention. This was achieved by 60.54% of subjects receiving Ferric carboxymaltose injection vs. 34.7% of subjects in the oral iron group (p<0.001). Mean haemoglobin change to day 56/end of study was 1.0 g/dL in the Ferric carboxymaltose injection group and 0.7 g/dL in the oral iron group (p=0.034, 95% CI: 0.0, 0.7).

Gastroenterology

Inflammatory bowel disease

Study VIT-IV-CL-008 was a randomised, open-label study which compared the efficacy of Ferric carboxymaltose injection vs. oral ferrous sulphate in reducing ID anaemia in subjects with inflammatory bowel disease (IBD). Subjects received either Ferric carboxymaltose injection (n=111) in single doses of up to 1,000 mg iron once per week until the individually

calculated iron dose (per Ganzoni formula) was reached (mean cumulative iron dose: 1,490 mg), or 100 mg iron BID as ferrous sulphate (n=49) for 12 weeks. Subjects receiving Ferric carboxymaltose injection showed a mean increase in Hb from baseline to Week 12 of 3.83 g/dL, which was non-inferior to 12 weeks of twice daily therapy with ferrous sulphate (3.75 g/dL, p=0.8016). Study FER-IBD-07-COR was a randomised, open-label study comparing the efficacy of Ferric carboxymaltose injection vs. iron sucrose in subjects with remitting or mild IBD. Subjects receiving Ferric carboxymaltose injection were dosed according to a simplified dosing grid using baseline Hb and body weight (see section 4.2) in single doses up to 1,000 mg iron, whereas subjects receiving iron sucrose were dosed according to individually calculated iron doses using the Ganzoni formula in doses of 200 mg iron until the cumulative iron dose was reached. Subjects were followed-up for 12 weeks. 65.8% of subjects receiving Ferric carboxymaltose injection (n=240; mean cumulative iron dose: 1,414 mg) vs. 53.6% receiving iron sucrose (n=235; mean cumulative dose 1,207 mg; p=0.004) had responded at Week 12 (defined as Hb increase ≥2 g/dL). 83.8% of Ferric carboxymaltose injection-treated subjects vs. 75.9% of iron sucrose-treated subjects achieved a Hb increase ≥2 g/dL or had Hb within normal limits at Week 12 (p=0.019).

Women's health

Post partum

Study VIT-IV-CL-009 was a randomised open-label non-inferiority study comparing the efficacy of Ferric carboxymaltose injection (n=227) vs. ferrous sulphate (n=117) in women suffering from post-partum anaemia. Subjects received either Ferric carboxymaltose injection in single doses of up to 1,000 mg iron until their individually calculated cumulative iron dose (per Ganzoni formula) was reached, or 100 mg of iron as oral ferrous sulphate BID for 12 weeks. Subjects were followed-up for 12 weeks. The mean change in Hb from baseline to Week 12 was 3.37 g/dL in the Ferric carboxymaltose injection group (n=179; mean cumulative iron dose: 1,347 mg) vs. 3.29 g/dL in the ferrous sulphate group (n=89), showing non-inferiority between the treatments.

Pregnancy

Intravenous iron medicines should not be used during pregnancy unless clearly necessary. Treatment with Ferric carboxymaltose injection should be confined to the second and third trimester if the benefit is judged to outweigh the potential risk for both the mother and the foetus.

Limited safety data in pregnant women are available from study FER-ASAP-2009-01, a randomised, open-label, study comparing Ferric carboxymaltose injection (n=121) vs. oral ferrous sulphate (n=115) in pregnant women in the second and third trimester with ID anaemia for a treatment period of 12 weeks. Subjects received Ferric carboxymaltose injection in cumulative doses of 1,000 mg or 1,500 mg of iron (mean cumulative dose: 1,029 mg iron) based on Hb and body weight at screening, or 100 mg of oral iron BID for 12 weeks. The incidence of treatment related adverse events was similar between Ferric carboxymaltose injection treated women and those treated with oral iron (11.4% Ferric carboxymaltose injection group; 15.3% oral iron group). The most commonly reported treatment-related adverse events were nausea, upper abdominal pain and headache. Newborn Apgar scores as well as newborn iron parameters were similar between treatment groups.

Paediatric population

Adolescents aged 14 years or older were included in 4 studies performed in adults. In addition, paediatric studies were performed in children and adolescents aged 1 to 17 years with iron deficiency anaemia. The most common aetiologies for iron deficiency anaemia were gastrointestinal diseases (e.g. inflammatory bowel disease, *Helicobacter pylori* gastritis,

coeliacic disease) and heavy uterine bleeding. In a prospective pharmacokinetic/pharmacodynamic phase 2 study (1VIT13036), 35 children at a median age of 9.8 years (range: 1.5-17.5 years) were treated in 2 consecutive dose cohorts with single doses of Ferric carboxymaltose injection 7.5 mg iron/kg body weight (n = 16) or Ferric carboxymaltose injection 15 mg iron/kg body weight (n = 19), at a maximum dose of 750 mg iron. Hb, ferritin and TSAT increased dose-dependently. On day 35 after injection, the mean (SD) increase in Hb was 1.9 (1.38) g/dL with Ferric carboxymaltose injection 7.5 mg iron/kg and 2.8 (1.15) g/dL with Ferric carboxymaltose injection 15 mg iron/kg. See also section 4.8. In a prospective, open-label, parallel-group phase 3 study (1VIT17044), efficacy and safety of Ferric carboxymaltose injection were compared with oral iron therapy. 40 children at a median age of 14.5 years (range:1 to 17 years) were treated with 2 doses of Ferric carboxymaltose injection 15 mg iron/kg body weight at a 7-day interval (maximum single dose 750 mg) and 39 children at a median age of 14.0 years (range: 1 to 17 years) with oral ferrous sulphate for 28 days. A similar increase in Hb was observed after both treatment with Ferric carboxymaltose injection and treatment with oral iron sulphate. The increase in Hb from baseline to day 35 (LS Mean [95%CI]) was 2.22 [1.69, 2.75] g/dL after Ferric carboxymaltose injection and 1.92 [1.43, 2.41] g/dL after oral iron sulphate. In total, 87.5% of patients in the intravenous iron group achieved a Hb increase >1 g/dL at EOS. The increase in ferritin and TSAT, used as a measure for the replenishment of iron stores, was higher after Ferric carboxymaltose injection therapy compared to oral iron sulphate therapy, with an increase in ferritin from baseline to day 35 (LS Mean [95%CI]) of 132.1 [105.44, 158.76] ng/mL after Ferric carboxymaltose injection and 11.0 [-15.62, 37.65] ng/mL after oral iron sulphate. The corresponding increase in TSAT was 24.3 [19.19, 29.41] % and 8.7 [3.70, 13.63] %, respectively.

Ferritin monitoring after replacement therapy

There is limited data from study VIT-IV-CL-008 which demonstrates that ferritin levels decrease rapidly 2-4 weeks following replacement and more slowly thereafter. The mean ferritin levels did not drop to levels where retreatment might be considered during the 12 weeks of study follow up. Thus, the available data does not clearly indicate an optimal time for ferritin retesting although assessing ferritin levels earlier than 4 weeks after replacement therapy appears premature. Thus, it is recommended that further re-assessment of ferritin should be made by the clinician based on the individual patient's condition.

5.3 Pharmacokinetic properties

Distribution

Positron emission tomography demonstrated that ^{59}Fe and ^{52}Fe from Ferric carboxymaltose injection was rapidly eliminated from the blood, transferred to the bone marrow, and deposited in the liver and spleen.

After administration of a single dose of Ferric carboxymaltose injection of 100 to 1,000 mg of iron in ID subjects, maximum total serum iron levels of 37 µg/mL up to 333 µg/mL are obtained after 15 minutes to 1.21 hours respectively. The volume of the central compartment corresponds well to the volume of the plasma (approximately 3 litres).

Elimination

The iron injected or infused was rapidly cleared from the plasma, the terminal halflife ranged from 7 to 12 hours, the mean residence time (MRT) from 11 to 18 hours. Renal elimination of iron was negligible.

Paediatric population

The pharmacokinetic properties of Ferric carboxymaltose injection at a dose of 15 mg iron/kg were similar to those for adult patients with iron deficiency. Serum iron increased proportionally to the dose after a single dose of 7.5 mg iron/kg or 15 mg iron/kg. After a single dose of Ferric carboxymaltose injection of 15 mg iron/kg body weight (maximum 750 mg), average maximum total serum iron values of 310 µg/mL were measured after 1.12 hours. The terminal halflife was 9.8 hours, and the distribution volume estimated by the population pharmacokinetic analysis was 0.42 to 3.14 l. Based on model-based simulations, the paediatrics subjects tended to have lower systemic exposure (lower AUC0-72h) compared to the adults (median per age group: 3,340 µg×h/mL (1 to 2 years), 4,110 µg×h/mL (3 to 12 years), 4,740 µg×h/mL (13 to 17 years), 8,864 µg×h/mL (adults)).

6 Nonclinical properties

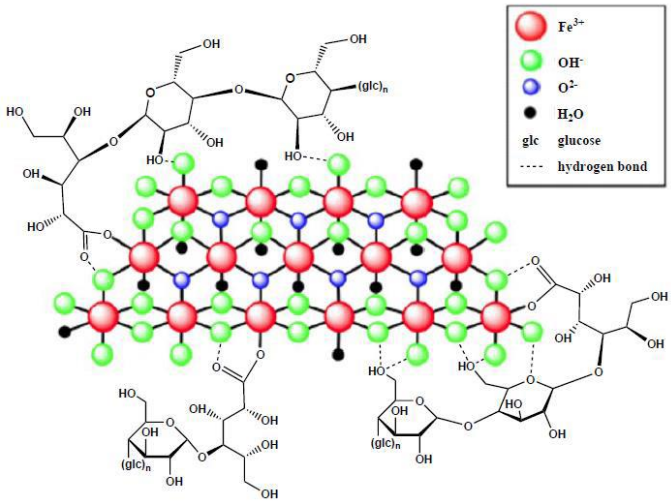
6.1 Animal Toxicology or Pharmacology

Preclinical data revealed no special hazard for humans based on conventional studies of safety pharmacology, repeat dose toxicity and genotoxicity. Preclinical studies indicate that iron released from Ferric carboxymaltose injection does cross the placental barrier, and is excreted in milk, in limited, controlled amounts. In reproductive toxicology studies using iron replete rabbits Ferric carboxymaltose injection was associated with minor skeletal abnormalities in the foetus at maternally toxic levels. In a fertility study in rats, there were no effects on fertility for either male or female animals. No long-term studies in animals have been performed to evaluate the carcinogenic potential of Ferric carboxymaltose injection. No evidence of allergic or immunotoxic potential has been observed. A controlled in-vivo test demonstrated no cross-reactivity of Ferric carboxymaltose injection with anti-dextran antibodies. No local irritation or intolerance was observed after intravenous administration.

7 Description

Ferric Carboxymaltose:

Ferric Carboxymaltose is Polynuclear iron (III)-hydroxide 4(R)-(Poly-(1-4)-O-α-D-glucopyranosyl)-oxy-2(R),3(S),5(R),6-tetrahydroxy-hexanoate. The empirical formula is $[FeO_x(OH)_y(H_2O)_z]_n$ $[\{C_6H_{10}O_5)_m$ $(C_6H_{12}O_7)\}1]$ks and its molecular weight is 150000 Da. The chemical structural formula is:



Redulid FCM

Ferric Carboxymaltose injection is Dark brown colloidal solution. The Excipients used are Sodium hydroxide solution and hydrochloric acid solution

8 Pharmaceutical particulars

8.1 Incompatibilities

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

8.2 Shelf-life

Do not use later than date of expiry.

8.3 Packaging information

REDULID FCM 100 is available in vial pack of 2 ml.

REDULID FCM 500 is available in vial pack of 10 ml

REDULID FCM 750 is available in vial pack of 15 ml

REDULID FCM 1000 is available in vial pack of 20 ml

8.4 Storage and handing instructions

Store below 30^0C. Do not Freeze.

Keep out of reach of children.

Before using. Check for absence of sediments.

Do not accept if vial seal is broken

9 Patient Counselling Information

Package leaflet: Information for the user

REDULID FCM

(Ferric Carboxymaltose Injection)

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.

What is in this leaflet

9.1 What REDULID FCM is and what it is used for

Ferric Carboxymaltose injection is Dark brown colloidal solution. The Excipients used are Sodium hydroxide solution and hydrochloric acid solution

It is used for the treatment of iron deficiency when oral iron preparations are ineffective or cannot be used.

9.2 What you need to know before you take

Do not take REDULID FCM

Contraindicated in cases of known hypersensitivity to Ferric Carboxymaltose Injection or to any of its excipients, known serious hypersensitivity to other parenteral iron products, anaemia not attributed to iron deficiency, e.g. other microcytic anaemia, evidence of iron overload or disturbances in utilization of iron and in pregnancy in the first trimester.

Warnings and precautions

Parenterally administered iron preparations can cause hypersensitivity reactions including anaphylactoid reactions,which may be potentially fatal. Therefore, facilities for cardio-pulmonary resuscitation must be available. Hypersensitivity reactions have also been reported after previously uneventful doses of parenteral iron complexes. The risk is enhanced for patients with known allergies including drug allergies, including patients with a history of severe asthma, eczema or other atopic allergy.

There is also an increased risk of hypersensitivity reactions to parenteral iron complexes in patients with immune or inflammatory conditions (e.g. systemic lupus erythematosus, rheumatoid arthritis).

Ferric Carboxymaltose Injection should only be administered when staff trained to evaluate and manage anaphylactic reactions is immediately available, in an environment where full resuscitation facilities can be assured. Each patient should be observed for adverse effects for at least 30 minutes following each Ferric Carboxymaltose Injection. If hypersensitivity reactions or signs of intolerance occur during administration, the treatment must be stopped immediately. Facilities for cardio respiratory resuscitation and equipment for handling acute anaphylactic/anaphylactoid reactions should be available, including an injectable 1:1000 adrenaline solution. Additional treatment with antihistamines and/or corticosteroids should be given as appropriate.

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 iş a precipitating factor, in particular Porphyria Cutanea Tarda (PCT). Careful monitoring of iron status is recommended to avoid iron overload. No safety data on haemodialysis-dependent chronic kidney disease patients receiving single doses of more than 200 mg iron are available.

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

Caution should be exercised to avoid paravenous leakage when administering Ferric Carboxymaltose Injection. Paravenous leakage of Ferric Carboxymaltose Injection at the injection site may lead to brown discolouration and irritation of the skin. In case of paravenous leakage, the administration of Ferric Carboxymaltose Injection must be stopped immediately.

The use of Ferric Carboxymaltose Injection has not been studied in children.

As with all parenteral iron preparations the absorption of oral iron is reduced when administered concomitantly.

9.3 How to take REDULID FCM

Ferric carboxymaltose must only be administered by the intravenous route:

- By injection, or
- By infusion, or,
- During a haemodialysis session undiluted directly into the venous limb of the dialyser.

Ferric carboxymaltose must not be administered by the subcutaneous or intramuscular route.

9.4 Possible side effects

The most commonly reported ADR is nausea (occurring in 3.1% of the patients), followed by headache, dizziness, and hypertension. Hypophosphataemia (common) may occur. The most serious ADR is anaphylactoid reactions with a frequency of rare.

9.5 How to store REDULID FCM

Store below 30ºC. Do not Freeze.

Keep out of reach of children.

Before using. Check for absence of sediments.

Do not accept if vial seal is broken.

9.6 Contents of the pack and other information

REDULID FCM Consists of Ferric Carboxymaltose as active ingredient.

The Excipients used are Sodium hydroxide solution and hydrochloric acid solution.

REDULID FCM 100 is available in vial pack of 2 ml.

REDULID FCM 500 is available in vial pack of 10 ml

REDULID FCM 750 is available in vial pack of 15 ml

REDULID FCM 1000 is available in vial pack of 20 ml

10 Details of manufacturer

Precise Biopharma Pvt. Ltd.

At.: Survey No. 46/1-4,

Village Kadaiya,

Nani Daman – 396 210

11 Details of permission or licence number with date

Mfg. Licence No.: DD/L/868 Issued on: 19.08.2023

12. Date of revision

NA

MARKETED BY

TORRENT PHARMACEUTICALS LTD.

Torrent House, Off Ashram Road,

Ahmedabad-380 009, INDIA

IN/REDULID FCM 50 mg/Aug-2023/01/PI