Hemoflux®

Ferric Carboxymaltose Injection

Composition
Hemoflux 500: Each 10mL Vial contains: Sterile solution of Ferric Carboxymaltose equivalent to 500 mg Elemental Iron (50 mg/mL).

Pharmacodynamic
Pharmacotherapeutic group: Iron trivalent, parenteral preparation, ATC code: B03AC
Hemoflux dispersion for injection/infusion is a colloidal solution of the iron complex ferric carboxymaltose. The complex is designed to provide, in a controlled way, utilizable iron for the iron transport and storage proteins in the body (transferrin and ferritin, respectively). Red cell utilization of 59Fe from radio-labelled Hemoflux 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. Its treatment results in an increase in reticulocyte count, serum ferritin levels and TSAT levels to within normal ranges.

Pharmacokinetic
After administration of a single dose 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).The iron injected or infused was rapidly cleared from the plasma, the terminal half-life ranged from 7 to 12 hours, the mean residence time (MRT) from 11 to 18 hours. Renal elimination of iron was negligible. Positron emission tomography demonstrated that Iron was rapidly eliminated from the blood, transferred to the bone marrow, and deposited in the liver and spleen.

Indications
Hemoflux injection 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.

Dosage and administration
The posology of Ferric Carboxymaltose follows a stepwise approach: (1) determination of the individual iron need, (2) calculation and administration of the iron dose(s), and (3) post-iron repletion assessments. These steps are outlined below:

Step 1: Determination of the iron need
The individual iron need for repletion using Hemoflux injection is determined based on the patient's body weight and haemoglobin (Hb) level. The following Table 1 for determination of the iron need:

Table 1: Determination of the iron need

	Patient body weight		
Hb (g/dl)	below 35 kg	35 kg to <70 kg	70 kg and over
<10	500 mg	1,500 mg	2,000 mg
10 to 14	500 mg	1,000 mg	1,500 mg
>14	500 mg	500 mg	500 mg

Note: Iron deficiency must be confirmed by laboratory tests

Step 2: Calculation and administration of the maximum individual iron dose(s)

Based on the iron need determined above the appropriate dose(s) of Ferric Carboxymaltose should be administered taking into consideration the following:

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)
- The maximum recommended cumulative dose of Ferric Carboxymaltose is 1,000 mg of iron per week.

Step 3: 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 utilization. In the event the patient requires further iron repletion, the iron need should be recalculated using Table 1 above.

Method of administrationIntravenous 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. The administration rates are as shown in Table 2:

Table 2: Administration rates for intravenous injection of Ferric Carboxymaltose

Volume of Ferric Carboxymaltose required	Equivalent iron dose	Administration rate / Minimum 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 / min
>10 to 20 mL	>500 to 1,000 mg	15 minutes

Intravenous Infusion: Ferric Carboxymaltose 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 1,000 mg iron. For infusion, Ferric Carboxymaltose must only be diluted in sterile 0.9% m/V sodium chloride solution as shown in Table 3.

Hemoflux injection must be administered only by Intravenous route: By bolus injection, or during a haemodialysis session undiluted directly into the venous limb of the dialyzer, or by drip infusion. In case of drip infusion Hemoflux injection must be diluted only in sterile 0.9% m/V sodium chloride solution as follows:

Table 3: Dilution plan of Hemoflux Injection for Intravenous infusion

Volume of Ferric Carboxymaltose required	Equivalent iron dose	Maximum amount of sterile 0.9% m/V sodium chloride solution	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 1,000 mg	250 mL	15 minutes

Note: For stability reasons, Ferric Carboxymaltose should not be diluted to concentrations less than 2 mg iron/mL. Ferric Carboxymaltose must not be administered by the subcutaneous or intramuscular route.

Special Population –Patients with 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 has not been studied in children, and therefore is not recommended in children under 14 years.

Contraindications: The use of Ferric Carboxymaltose is contraindicated in cases of:
- Hypersensitivity to the active substance, to Ferric Carboxymaltose or 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 the utilization of iron

Special warnings and precautions for use
Serious hypersensitivity reactions, including anaphylactic-type reactions, some of which have been life-threatening and fatal, have been reported in patients receiving Ferric Carboxymaltose. Patients may present with shock, clinically significant hypotension, loss of consciousness and collapse. Monitor patients for signs and symptoms of hypersensitivity during and after Ferric Carboxymaltose administration for at least 30 minutes and until clinically stable following completion of the infusion. Only administer Ferric Carboxymaltose when personnel and therapies are immediately available for the treatment of serious hypersensitivity reactions. Other serious or severe adverse reactions potentially associated with hypersensitivity which included, but not limited to, pruritus, rash, urticaria, wheezing, or hypotension may occur.

Hypertension
Transient elevations in systolic blood pressure, sometimes occurring with facial flushing, dizziness, or nausea may be occurred. These elevations generally occurred immediately after dosing and resolved within 30 minutes. Monitor patients for signs and symptoms of hypertension following each Ferric Carboxymaltose administration.

Laboratory Test Alterations
In the 24 hours following administration of Ferric Carboxymaltose, laboratory assays may overestimate serum iron and transferrin bound iron by also measuring the iron in Ferric Carboxymaltose.Interaction with other medicinal products and other forms of interaction: 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 Hemoflux injection.

Fertility, pregnancy and lactation

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. Animal data suggest that iron released from Hemoflux injection can cross the placental barrier and that its use during pregnancy may influence skeletal development in the fetus 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 fetus.

Lactation: Based on limited data on breast-feeding women it is unlikely that Ferric Carboxymaltose represents a risk to the breast-fed child.

Fertility was unaffected following treatment in animal studies

Undesirable effects
The side effects of Ferric Carboxymaltose are infrequent, usually mild & generally do not cause patients to stop treatment. The most common side effect is nausea, followed by headache, dizziness, and hypertension, injection site reactions, nausea, alanine aminotransferase increased, hypophosphataemia. Uncommon side effects are hypersensitivity, dysgeusia, tachycardia, hypotension, flushing, dyspnoea, dyspepsia, abdominal pain, constipation, diarrhea, Pruritus, urticaria, erythema, rash, myalgia, back pain, arthralgia, muscle spasms, Pyrexia, fatigue, chest pain, oedema peripheral, chills, aspartate aminotransferase increased, gamma-glutamyl transferase increased, blood lactate dehydrogenase increased, blood alkaline phosphatase increased. Rare side effects are anaphylactoid reactions, loss of consciousness, anxiety, phlebitis, syncope, presyncope, bronchospasm, flatulence, angioedema, pallor, and face oedema, rigors, malaise, influenza like illness.

Overdose
Excessive dosages of Ferric Carboxymaltose may lead to accumulation of iron in storage sites potentially 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.

Storage Conditions: Do not store above 30°C.Protect from direct sunlight. Keep out of the reach of children. Do not freeze.

Shelf-life: 2 years

Presentation: A Vial of sterile solution of Ferric Carboxymaltose Injection, 100 mL sterile solution of 0.9%w/v Sodium Chloride (Normal Saline), infusion set, complementary pouch (sterile 10 mL disposable syringe with needle, alcohol pad, first aid bandage & butterfly needle).

Distribution category: Prescription Only Medicine (POM).

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Size: 8.7" x 13"