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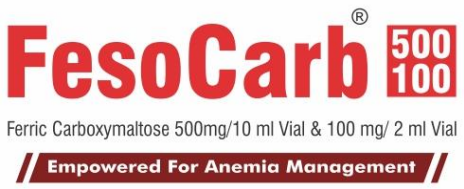
Maximising Life



Product Description:

- **Fesocarb 500**: Available in 10 ml vial. Each ml contains Ferric Carboxymaltose 50mg. Ferric Carboxymaltose 500 mg/10 ml vial
- **Fesocarb 100**: Available in 2 ml vial. Each ml contains Ferric Carboxymaltose 50mg. Ferric Carboxymaltose 100 mg/2 ml vial

Description:
Ferric Carboxymaltose is a dark brown, sterile, aqueous solution for intravenous injection. It is an anti-anemic medication.

Indications:
FesoCarb is indicated for the treatment of iron deficiency anemia 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.

CLINICAL PHARMACOLOGY: -

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

Pharmacodynamics Using positron emission tomography (PET) it was demonstrated that red cell uptake of ^{59}Fe and ^{52}Fe from Fesocarb ranged from 61% to 99%. In patients with iron deficiency, red cell uptake of radio-labeled iron ranged from 91% to 99% at 24 days after Fesocarb dose. In patients with renal anemia red cell uptake of radio-labeled iron ranged from 61% to 84% after 24 days Fesocarb dose.

Pharmacokinetics After administration of a single dose of Fesocarb of 100 to 1000 mg of iron in iron deficient patients, maximum iron concentration of 37 µg/mL to 333 µg/mL were obtained respectively after 15 minutes to 1.21 hours post dose. The volume of distribution was estimated to be 3 L.

The iron injected or infused was rapidly cleared from the plasma, the terminal half-life ranged from 7 to 12 hours. Renal elimination of iron was negligible.

Dosage:
The diagnosis of iron deficiency must be based on laboratory tests.

Step 1: Determination of the iron need

The individual iron need for repletion using FesoCarb is determined based on the patient's body weight and haemoglobin (Hb) level. Refer to Table 1 for determination of the total iron need. 2 doses may be required to replenish the total iron need.

Table 1: Determination of the total iron need

Hb	**Patient body weight**		
g/dL	**Below 35 kg**	**35 kg to <70 kg**	**70 kg and above**
<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

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

Based on the total iron need determined, the appropriate dose(s) of FesoCarb should be administered taking into consideration the following:

Adults and adolescents aged 14 years and older

A single FesoCarb 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 FesoCarb)

The maximum recommended cumulative dose of FesoCarb is 1,000 mg of iron (20 mL FesoCarb) per week. 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.

Paediatric Patients: The use of Ferric Carboxymaltose injection has not been studied in children and therefore has not recommended in children under 14 years

Method of administration

FesoCarb 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.

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

Intravenous injection

FesoCarb may be administered by intravenous injection using undiluted dispersion. In adults and adolescents aged 14 years and older, the maximum single dose is 15 mg iron/kg body weight but should not exceed 1,000 mg of iron.

Table 2: Administration rates for intravenous injection of FesoCarb

Ferric Carboxymaltose	Equivalent Iron Dose	Administration rate / Minimum administration time
2- 4 ml	100- 200 mg	No minimal prescribed time
>4 – 10 ml	>200- 500 mg	100 mg iron / min
>10- 20 ml	>500- 1000 mg	15 minutes

Intravenous infusion

FesoCarb may be administered by intravenous infusion, in which case it must be diluted. In adults and adolescents aged 14 years and older, the maximum single dose is 20 mg iron/kg body weight, but should not exceed 1,000 mg of iron.

For infusion, FesoCarb must only be diluted in sterile 0.9% m/V sodium chloride solution. Note: for stability reasons, FesoCarb should not be diluted to concentrations less than 2 mg iron/mL (not including the volume of the ferric carboxymaltose dispersion). For further instructions on dilution of the medicinal product before administration.

Table 3: Dilution plan of FesoCarb for intravenous infusion

Ferric Carboxymaltose	Equivalent Iron Dose	Maximum amount of sterile 0.9% NaCL solution 50 ml/100 ml	Administration rate / Minimum administration time
2- 4 ml	100- 200 mg	50 ml	No minimal prescribed time
>4 – 10 ml	>200- 500 mg	100 ml	100 mg iron / min
>10- 20 ml	>500- 1000 mg	250 ml	15 minutes

Administration:

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

FesoCarb 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 FesoCarb administration.

Contraindications:

The use of FesoCarb is contraindicated in cases of:

• hypersensitivity to the active substance, to FesoCarb 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 utilisation of iron.

Warnings And Precautions:

Hypersensitivity reactions

Parenterally administered iron preparations can cause hypersensitivity reactions including serious and potentially fatal anaphylactic reactions. Hypersensitivity reactions have also been reported after previously uneventful doses of parenteral iron complexes. There have been reports of hypersensitivity reactions which progressed to Kounis syndrome (acute allergic coronary arteriospasm that can result in myocardial infarction.

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).

FesoCarb should only be administered when staff trained to evaluate and manage anaphylactic reactions are 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 FesoCarb administration. 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 reactions should be available, including an injectable 1:1000 adrenaline solution. Additional treatment with antihistamines and/or corticosteroids should be given as appropriate.

Hypophosphataemic osteomalacia

Symptomatic hypophosphataemia leading to osteomalacia and fractures requiring clinical intervention including surgery has been reported in the post marketing setting. Patients should be asked to seek medical advice if they experience worsening fatigue with myalgias or bone pain. Serum phosphate should be monitored in patients who receive multiple administrations at higher doses or long-term treatment, and those with existing risk factors for hypophosphataemia. In case of persisting hypophosphataemia, treatment with ferric carboxymaltose should be re-evaluated.

Hepatic or renal impairment

In patients with liver dysfunction, parenteral iron should only be administered after careful benefit/risk 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). 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.

Infection

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

Extravasation

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

Excipients

FesoCarb contains up to 5.5 mg (0.24 mmol) sodium per mL of undiluted dispersion, equivalent to 0.3% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

Drug Interactions:
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 FesoCarb.

Use In Special population
Pregnancy:
There are limited data from the use of FesoCarb in pregnant women . A careful benefit/risk evaluation is required before use during pregnancy and FesoCarb 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. Treatment with FesoCarb 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.

Foetal bradycardia may occur following administration of parenteral irons. It is usually transient and a consequence of a hypersensitivity reaction in the mother. The unborn baby should be carefully monitored during intravenous administration of parenteral irons to pregnant women.

Animal data suggest that iron released from FesoCarb can cross the placental barrier and that its use during pregnancy may influence skeletal development in the fetus (see section 5.3).

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

Fertility

There are no data on the effect of FesoCarb on human fertility. Fertility was unaffected following FesoCarb treatment in animal studies

Adverse Reactions:

System Organ Class	Common	Uncommon	Rare	Frequency not known
Immune system disorders		Hypersensitivity	Anaphylactic reactions	
Metabolism and nutritional disorders	Hypophosphataemia			
Gastrointestinal disorders	Nausea	Abdominal pain, vomiting, constipation, diarrhoea, dyspepsia	Flatulence	
Cardiac disorders		Tachycardia		
Skin and subcutaneous tissue disorders		Rash, pruritus, urticaria, erythema	distant skin discolouration, pallor	Face oedema
General disorders and administration site conditions	Injection/infusion site reactions	fatigue, chills, chest pain, oedema	Influenza like illness (whose onset may vary from a few hours to several days)	

Overdose:

Administration of FesoCarb 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 (TSAT) may assist in recognising iron accumulation. If iron accumulation has occurred, treat according to standard medical practice, e.g. consider the use of an iron chelator.

Shelf Life:

Shelf life of the product as packaged for sale: 2 years.

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:

From a microbiological point of view, preparations for parenteral administration should be used immediately after dilution with sterile 0.9% m/V sodium chloride solution.

Storage:
Store in the original package in order to protect from light. Do not store above 30 °C. Do not freeze.