For Medical Professional only

Boferin™ Injection 500mg/10ml
(Ferric Carboxymaltose)

بوفرین ۵۰۰ ملی گرام/۱۰ ملی لیٹر انجکشن
(فیرک کاربوکسی مالٹوز)

DESCRIPTION:
Ferric carboxymaltose, an iron replacement product, is an iron carbohydrate complex with the chemical name of polynuclear iron (III) hydroxide 4(R)-(poly-(1→4)-O-α-D-glucopyranosyl)-oxy-2(R),3(S),5(R),6-tetrahydroxy-hexanoate. It has a relative molecular weight of approximately 150,000 Da corresponding to the following empirical formula: $[FeOx(OH)y(H_2O)z]n[\{(C_6H_{10}O_5)m(C_6H_{12}O_7)\}l]k$, Where $n \approx 10^3$, $m \approx 8$, $l \approx 11$, and $k \approx 4$ (l represents the mean branching degree of the ligand).

Ferric carboxymaltose injection is a dark brown, sterile, aqueous, isotonic colloidal solution for intravenous injection.

COMPOSITION:
Each 10mL vial contains:
Iron (as ferric carboxymaltose)....500mg
(Product Specs.: Innovator's)

CLINICAL PHARMACOLOGY:
Pharmacodynamic Properties:
Pharmacotherapeutic group: Iron trivalent, parenteral preparation
ATC code: B03AC

Mechanism of Action
Boferin solution 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 ^{59}Fe from radio-labelled Boferin 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. Boferin treatment results in an increase in reticulocyte count, serum ferritin levels and TSAT levels to within normal ranges.

Pharmacokinetic Properties
Distribution:
Positron emission tomography demonstrated that ^{59}Fe and ^{52}Fe from Boferin 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 Boferin 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 half-life ranged from 7 to 12 hours, the mean residence time (MRT) from 11 to 18 hours. Renal elimination of iron was negligible.

THERAPEUTIC INDICATIONS:
Boferin 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:
Monitor carefully patients for signs and symptoms of hypersensitivity reactions during and following each administration of Boferin.

Boferin 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 Boferin administration.

Posology
The posology of Boferin follows a stepwise approach:

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

Hb		Patient body weight		
g/dL	mmol/L	below 35 kg	35 kg to <70 kg	70 kg and above
<10	<6.2	500 mg	1,500 mg	2,000 mg
10 to <14	6.2 to <8.7	500 mg	1,000 mg	1,500 mg
≥14	≥8.7	500 mg	500 mg	500 mg

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 Boferin should be administered taking into consideration the following:
A single Boferin 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 Boferin)

The maximum recommended cumulative dose of Boferin is 1,000 mg of iron (20 mL Boferin) 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 Boferin administration to allow adequate time for erythropoiesis and iron utilisation. In the event the patient requires further iron repletion, the iron need should be recalculated using Table 1.

Patients with haemodialysis-dependent chronic kidney disease:
A single maximum daily dose of 200 mg iron should not be exceeded in haemodialysis-dependent chronic kidney disease patients

Paediatric population:
The use of Boferin has not been studied in children, and therefore is not recommended in children under 14 years.

Method of Administration:
Boferin 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.

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

Intravenous injection
Boferin 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 Boferin

Volume of Boferin 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
Boferin 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, Boferin must only be diluted in sterile 0.9% m/V sodium chloride solution as shown in Table 3. Note: for stability reasons, Boferin should not be diluted to concentrations less than 2 mg iron/mL (not including the volume of the ferric carboxymaltose solution).

Table 3: Dilution plan of Boferin for intravenous infusion

Volume of Boferin 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	No minimal prescribed time
>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

CONTRAINDICATIONS:
The use of Boferin is contraindicated in cases of:
- Hypersensitivity to the active substance, to Boferin 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/anaphylactoid 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).

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.

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 Boferin 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 Boferin. Paravenous leakage of Boferin 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 Boferin must be stopped immediately.

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 Boferin.

ADVERSE EFFECTS:

Common:

Hypophosphataemia, headache, dizziness, flushing, hypertension, nausea, injection/infusion site reactions.

Uncommon:

Hypersensitivity, paraesthesia, dysgeusia, tachycardia, hypotension, dyspnoea, vomiting, dyspepsia, abdominal pain, constipation, diarrhea, pruritus, urticaria, erythema, rash, myalgia, back pain, arthralgia, pain in extremity, muscle spasms, pyrexia, fatigue, chest pain, oedema peripheral, chills.

Rare:

Anaphylactoid/anaphylactic reactions, anxiety, phlebitis, syncope, presyncope, bronchospasm, flatulence, angioedema, pallor, distant skin discolouration, malaise, influenza like illness (whose onset may vary from a few hours to several days).

Not Known:

Loss of consciousness, kounis syndrome, face oedema, hypophosphataemic osteomalacia.

USE IN PREGNANCY AND LACTATION:

Pregnancy:

There are limited data from the use of Boferin in pregnant women. A careful benefit/risk evaluation is required before use during pregnancy and Boferin 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 Boferin 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.

Boferin can cross the placental barrier and that its use during pregnancy may influence skeletal development in the fetus.

Lactation:

Transfer of iron from Boferin to human milk was negligible (≤1%). Based on limited data on breast-feeding women it is unlikely that Boferin represents a risk to the breast-fed child.

OVERDOSE:

Administration of Boferin 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, treat according to standard medical practice, e.g. consider the use of an iron chelator.

SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING:

Inspect vials visually for sediment and damage before use. Use only those containing sediment-free, homogeneous solution.
Each vial of Boferin is intended for single use only.
Boferin 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.

SHELF LIFE

2 years

STORAGE:

Protect from heat & sunlight, store below 30°C.
The expiration date refer to the product correctly stored at the required condition. Do not freeze.
Keep out of the reach of children.
Preparations for parenteral administration should be used immediately.
Patients and healthcare professionals can also report suspected adverse drug reaction at ade@bosch-pharma.com.
To be sold on the prescription of registered medical practitioner only.

PRESENTATION:

As per mentioned in pack size

صرف وریدی استعمال کے لیے:

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

ہدایات: گرمی اور روشنی سے محفوظ ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
منجمد ہونے سے محفوظ رکھیں۔ بچوں کی پہنچ سے دور رکھیں۔
صرف مستند ڈاکٹر کے نسخے پر فروخت کے لئے۔

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