Ferotein™-S
(Iron Sucrose)

فیروٹین۔ایس

100mg/5mL Solution for Injection

DESCRIPTION
Iron Sucrose injection is a brown, sterile, aqueous, complex of polynuclear iron (III)-hydroxide in sucrose for intravenous use.

QUALITATIVE AND QUANTITATIVE COMPOSITION
FEROTEIN-S (Iron sucrose) Injection 100mg/5mL

Each 5mL contains:
Elemental iron …… 100mg
(as iron sucrose)

CLINICAL PHARMACOLOGY
Pharmacokinetics
Absorption
In intravenous doses of iron sucrose, its iron component exhibits first order kinetics with an elimination half-life of 6 hours, total clearance of 1.2L/hr, non-steady state apparent volume of distribution of 10L and steady state apparent volume of distribution of 7.9L. Since iron disappearance from serum depends on the need for iron in the iron stores and iron utilizing tissues of the body, serum clearance of iron is expected to be more rapid in iron deficient patients treated with iron sucrose as compared to healthy individuals.

Distribution
In intravenous doses of iron sucrose, its iron component appears to distribute mainly in blood and to some extent in extravascular fluid. The volume of distribution at steady state is about 8L, indicating a low iron distribution in the body fluid.

Metabolism & Excretion
Following intravenous administration, iron sucrose is dissociated into iron and sucrose by the reticuloendothelial system. Renal elimination of iron occurring in the first 4 hours after injection correspond to less than 5% of the total body clearance. After 24 hours the plasma levels of iron were reduced to the pre-dose level and about 75% of the dosage of sucrose was excreted.

THERAPEUTIC INDICATIONS
FEROTEIN-S (Iron sucrose) is indicated for the treatment of iron deficiency in the following:
- Where there is a clinical need to deliver iron rapidly to iron stores.
- Patients who cannot tolerate oral iron therapy or who are non-compliant.
- In active inflammatory bowel disease where oral iron preparations are ineffective.
- Non-dialysis dependent-chronic kidney disease (NDD-CKD) patients receiving an erythropoietin.
- Non-dialysis dependent-chronic kidney disease (NDD-CKD) patients not receiving an erythropoietin.
- Hemodialysis dependent-chronic kidney disease (HDD-CKD) patients receiving an erythropoietin.
- Peritoneal dialysis dependent-chronic kidney disease (HDD-CKD) patients receiving an erythropoietin.

DOSAGE AND ADMINISTRATION
Dosage
Adults and the elderly: The total cumulative dose of FEROTEIN-S (Iron sucrose), equivalent to the total iron deficit (mg), is determined by the hemoglobin level and body weight. The dose for FEROTEIN-S (Iron sucrose) must be individually determined for each patient according to the total iron deficit calculated with the following formula:

Total iron deficit [mg] = body weight [kg] x (target Hb - actual Hb) [g/L] x 0.24* + depot iron [mg]

- Below 35 kg body weight: target Hb = 130g/L and depot iron=15mg/kg body weight
- 35 kg body weight and above: target Hb=150g/L and depot iron=500mg

* Factor 0.24 = 0.0034 x 0.07 x 1000 (Iron content of hemoglobin 0.34%; Blood volume 7% of body weight; Factor 1000 = conversion from g to mg)

Total amount of FEROTEIN-S (Iron sucrose) to be administered (in mL) = $\frac{\text{Total iron deficit (mg)}}{\text{20mg/mL}}$

The total amount of FEROTEIN-S (Iron sucrose) required is determined from either the above calculation or the following dosage table:

Body Weight (kg)	Total number of FEROTEIN-S (Iron sucrose) ampoules to be administered (1 ampoule of FEROTEIN-S (Iron sucrose) corresponds to 5mL)			
	Hb 60g/L	Hb 75g/L	Hb 90g/L	Hb 105g/L
5	1.5	1.5	1.5	1
10	3	3	2.5	2
15	5	4.5	3.5	3
20	6.5	5.5	5	4
25	8	7	6	5.5
30	9.5	8.5	7.5	6.5
35	12.5	11.5	10	9
40	13.5	12	11	9.5
45	15	13	11.5	10
50	16	14	12	10.5
55	17	15	13	11
60	18	16	13.5	11.5
65	19	16.5	14.5	12
70	20	17.5	15	12.5
75	21	18.5	16	13
80	22.5	19.5	16.5	13.5
85	23.5	20.5	17	14
90	24.5	21.5	18	14.5

To convert Hb (mM) to Hb (g/L), multiply the former by 16.1145.

The usual dosage is 5-10mL FEROTEIN-S (Iron sucrose) (100-200mg iron) one to three times a week depending on the hemoglobin level.

Children
If there is a clinical need, it is recommended not to exceed 0.15mL FEROTEIN-S (Iron sucrose) (3mg iron) per kg one to three times per week depending on the hemoglobin level.

Maximum Dose:
Intravenous Infusion
The maximum tolerated single dose is 7mg iron per kg body weight given once per week, but not exceeding 500mg iron.

Intravenous Injection
The maximum allowed single dose is 200mg iron. If the total necessary dose exceeds the maximum allowed single dose, then the administration has to be split.

CKD Patients
Most CKD patients will require a minimum cumulative repletion dose of 1,000mg of elemental iron, administered over sequential sessions, to achieve a favourable hemoglobin response and to replenish iron stores (ferritin, TSAT). Hemodialysis patients may continue to require therapy with FEROTEIN-S (Iron sucrose) or other intravenous iron preparations at the lowest dose necessary to maintain target levels of haemoglobin.

Hemodialysis Dependent-Chronic Kidney Disease Patients (HDD-CKD): FEROTEIN-S (Iron sucrose) may be administered undiluted as a 100mg slow intravenous injection over 2 to 5 minutes or as an infusion of 100mg, diluted in a maximum of 100mL of 0.9% NaCl over a period of at least 15 minutes per consecutive hemodialysis session for a total cumulative dose of 1000mg.

Non-Dialysis Dependent-Chronic Kidney Disease Patients (NDD-CKD): FEROTEIN-S (Iron sucrose) is administered as a total cumulative dose of 1000mg over a 14 day period as a 200mg slow IV injection undiluted over 2 to 5 minutes on 5 different occasions within the 14 day period.

Peritoneal Dialysis Dependent-Chronic Kidney Disease Patients (PDD-CKD): FEROTEIN-S (Iron sucrose) is administered as a total cumulative dose of 1000mg in 3 divided doses, given by slow

intravenous infusion, within a 28 day period: 2 infusions of 300mg over 1.5 hours 14 days apart followed by one 400mg infusion over 2.5 hours 14 days later. The FEROTEIN-S (Iron sucrose) dose should be diluted in a maximum of 250mL of 0.9% NaCl.

Administration:
FEROTEIN-S (Iron sucrose) must only be administered by the intravenous route. This may be by slow intravenous injection or by an intravenous drip infusion. Before administering the first dose to a new patient, a test dose of FEROTEIN-S (Iron sucrose) should be given.
FEROTEIN-S (Iron sucrose) must not be used for intramuscular injection.
Do not administer if sedimentation observed.

Intravenous Infusion
The infusion times must be strictly adhered to, even if the patient does not receive the maximum tolerated single dose.
Before administering the infusion, the first 25mg of iron (i.e., 25mL of solution) should be infused as a test dose over a period of 15 minutes. If no adverse reactions occur during this time then the remaining portion of the infusion should be given at an infusion rate of not more than 50mL in 15 minutes.
FEROTEIN-S (Iron sucrose) must be diluted only in sterile 0.9% w/v sodium chloride solution.
- 5mL (100mg) of FEROTEIN-S (Iron sucrose) should be diluted in max 100mL sterile 0.9% w/v sodium chloride solution.
- 10mL (200mg) of FEROTEIN-S (Iron sucrose) should be diluted in max 200mL sterile 0.9% w/v sodium chloride solution.

For stability reasons FEROTEIN-S (Iron sucrose) must be diluted only in sterile 0.9% w/v sodium chloride solution.
Dilution must take place immediately prior to infusion and the solution should be administered as follows:
- 100mg iron (5mL of FEROTEIN-S (Iron sucrose)) in at least 15 minutes.
- 200mg iron (10mL of FEROTEIN-S (Iron sucrose)) in at least 30 minutes.
- 300mg iron (15mL of FEROTEIN-S (Iron sucrose)) in at least 1• hours.
- 400mg iron (20mL of FEROTEIN-S (Iron sucrose)) in at least 2• hours.

The maximum tolerated single dose given not more than once per week is:
- Patients above 70kg: 500mg iron (25mL FEROTEIN-S (Iron sucrose)) in at least 3• hours.
- Patients of 70kg and below: 7mg iron/kg body weight in at least 3• hours.

Intravenous Injection
This may be by a slow intravenous injection at a rate of 1mL undiluted solution per minute (i.e., 5 minutes per ampoule) and not exceeding 2 ampoules FEROTEIN-S (Iron sucrose) (200mg iron) per injection. Before administering a slow intravenous injection, a test dose of 1mL (20mg of iron) should be injected slowly over a period of 1 to 2 minutes. If no adverse events occur within 15 minutes of completing the test dose, then the remaining portion of the injection may be given.

Injection into dialyser:
FEROTEIN-S (Iron sucrose) may be administered during a hemodialysis session directly into the venous limb of the dialyser under the same procedures as those outlined for intravenous injection.

ADVERSE REACTIONS
Following adverse drug reactions have been reported:

Common: transient taste perversions (in particular metallic taste).

Uncommon: headache, dizziness, hypotension and collapse, tachycardia, palpitations, bronchospasm, dyspnea, nausea, vomiting, abdominal pain, diarrhea pruritus, urticaria, rash, exanthema, erythema, muscle cramps, myalgia, fever, shivering, flushing, chest pain and tightness. Injection site disorders such as superficial phlebitis, burning, swelling.

Rare: paresthesia, anaphylactoid reactions (rarely involving arthralgia), peripheral edema, fatigue, asthenia, malaise.

Isolated cases: reduced level of consciousness, light-headed feeling, confusion, angioedema, swelling of joints, hyperhidrosis and back pain.

Hemodialyis dependent-chronic kidney disease (HDD-CKD) patients: hypotension, muscle cramps, nausea, headache, graft complications, vomiting, dizziness, hypertension, chest pain and diarrhea.

Non-dialysis dependent-chronic kidney disease (NDD-CKD) patients: dysgeusia, peripheral edema, diarrhea, constipation, nausea, dizziness and hypertension.

Patients receiving erythropoietin may experience: diarrhea, edema, nausea, vomiting, arthralgia, back pain, headache, hypertension, dysgeusia, dizziness, extremity pain and injection site burning.

Peritoneal dialysis dependent-chronic kidney disease (PDD-CKD) patients: diarrhea, peritoneal infection, vomiting, hypertension, pharyngitis, peripheral edema and nausea.

CONTRAINDICATIONS
The use of iron sucrose is contra-indicated in cases of:
- Known hypersensitivity to iron sucrose or any of its components.
- Anemias not attributable to iron deficiency.
- Iron overload or disturbances in utilization of iron.
- Patients with a history of asthma, eczema or other atopic allergy, because they are more susceptible to experience allergic reactions.
- Pregnancy first trimester.

PRECAUTIONS
- Parenteral administered iron preparations can cause allergic or anaphylactoid reactions, which may be potentially fatal. Therefore, treatment for serious allergic reactions and facilities with the established cardio-pulmonary resuscitation procedures should be available.
- 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). Careful monitoring of iron status is recommended to avoid iron overload.
- Parenteral iron must be used with caution in case of acute or chronic infection. It is recommended that the administration of iron sucrose 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.
- Hypotensive episodes may occur if the injection is administered too rapidly. Allergic reactions, sometimes involving arthralgia, have been more commonly observed when the recommended dose is exceeded.
- Paravenous leakage must be avoided because leakage of iron sucrose at the injection site may lead to pain, inflammation, tissue necrosis and brown discoloration of the skin.

Pregnancy
Iron sucrose should be used during pregnancy catagory B only if the potential benefit justifies the potential risk to mother and fetus.

Nursing Mothers
It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk caution should be exercised when iron sucrose is administered to a nursing women.

Drug Interactions
As with all parenteral iron preparations, iron sucrose should not be administered concomitantly with oral iron preparations since the absorption of oral iron is reduced. Therefore, oral iron therapy should be started at least 5 days after the last injection of Iron Sucrose.

OVERDOSAGE
Overdosage can cause acute iron overloading which may manifest itself as hemosiderosis. Overdosage should be treated with supportive measures and, if required, with an iron chelating agent.

STORAGE
Store at 25°C (Excursions permitted between 15°C - 30°C).
Protect from light & heat.
Do not freeze.
The expiration date refers to the product correctly stored at the required conditions.

HOW SUPPLIED
FEROTEIN-S (Iron sucrose) injection 100mg/5mL is available as 5 ampoules.

Keep out of reach of children.

To be sold on prescription of a registered medical practitioner only.

Please read the contents carefully before use.
This package insert is continually updated from time to time.

Manufactured by:
Getz pharma (PVT) LIMITED
www.getzpharma.com
29-30/27, K.I.A., Karachi, Pakistan
Rev. Mar, 2010
L01 - 200004080