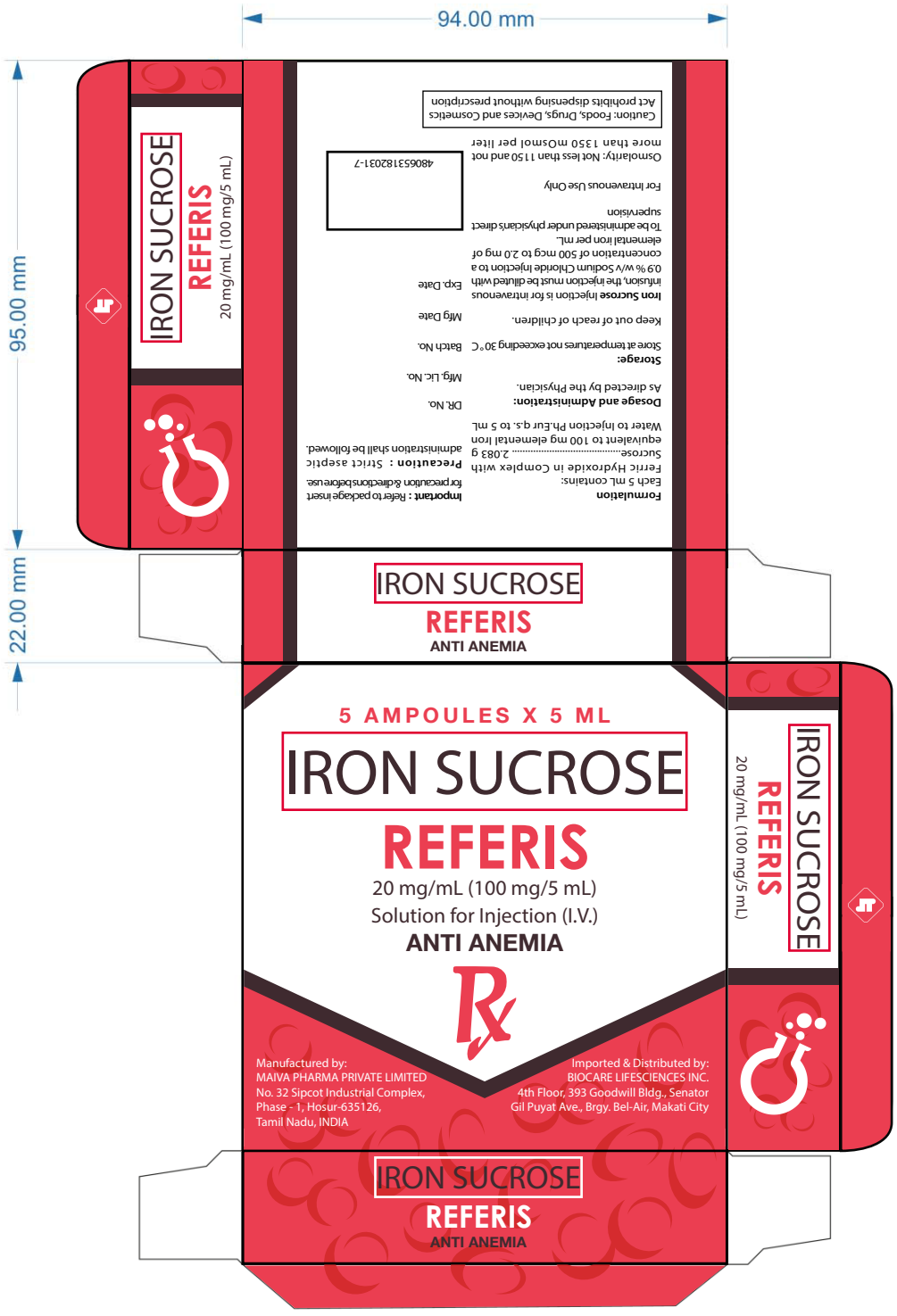

Specification box					
Market : Export			Artist :		
Product name : Iron Sucrose Injection (5 x 5 mL)			Varnish : Un-Varnish area for batch details		
Item : Carton			Manufactured by : Global Pharmatech		
Size: 94 x 95 mm			Date : 27 / 01/ 17		
Artwork Code:					
Color :					
Prepared packaging department	Checked by Regulatory Affairs	Checked by Bussiness development	Checked by Quality Assurance	Checked by Quality control	Checked by Quality Operations
Reason for change :					

IRON SUCROSE
REFERIS

℞

5 mL

20 mg / mL (100 mg/ 5 mL) Solution for Injection (I.V.)
Anti-Anemia

Formulation
Each 5 mL contains:
Ferric Hydroxide in Complex with Sucrose..... 2.083 g
equivalent to 100 mg elemental Iron
Water to Injection Ph.Eur q.s. to 5 mL

Dosage and Administration:
As directed by the Physician.

Storage:
Store at temperatures not exceeding 30 °C

Keep out of reach of children.

Iron Sucrose Injection is for intravenous infusion, the injection must be diluted with 0.9 % w/v Sodium Chloride Injection to a concentration of 500 mcg to 2.0 mg of elemental iron per mL.
To be administered under physician's direct supervision

Important: Refer to package insert precaution & directions before use.

Precaution: Strict aseptic administration shall be followed.

Caution: Before using check for absence of sediments. The injection should be discarded if any visible particles appears.

Osmolarity: Not less than 1150 and not more than 1350 mOsmol per liter

Caution: Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription

DR. No.
Mfg. Lic. No.
Batch No.
Mfg Date
Exp. Date

Manufactured by:
MAIVA PHARMA PRIVATE LIMITED
No. 32 Sipcot Industrial Complex,
Phase - 1, Hosur-635126,
Tamil Nadu, INDIA

Imported & Distributed by:
BIOCARE LIFESCIENCES INC.
4th Floor, 393 Goodwill Bldg., Senator
Gil Puyat Ave., Brgy. Bel-Air, Makati City

480653182031-7

80.00 mm

208.00 mm

For the use of a registered medical practitioner or a hospital or a laboratory only

IRON SUCROSE

Referis

℞

20 mg / mL (100 mg / 5mL) Solution for Injection (I.V.)
Anti-Anemia

Therapeutic Category: Iron supplement.

Formulation:
Each 5mL contains:
Ferric Hydroxide in Complex with Sucrose .....2.083 g
equivalent to 100mg Elemental Iron
Water for Injection Ph.Eur q.s. to 5mL

Description:
A homogeneous brown liquid, free from particulate matter filled with 5 mL in flint ampoules with purple snap off, USP Type-I.

Clinical Pharmacology:
Pharmacodynamics:
Following intravenous administration of Iron sucrose is dissociated by the reticuloendothelial system into iron and sucrose. **Pharmacokinetics:** In healthy adults treated with intravenous doses of Iron sucrose (Referis) injection, its iron component exhibits first order kinetics with an elimination half-life of 6h, total clearance of 1.2L/h, non-steady state apparent volume of distribution of 10.0L 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 utilising tissues of the body, serum clearance of iron is expected to be more rapid in iron deficient patients treated with Iron sucrose injection as compared to healthy individuals. The effects of age and gender on the pharmacokinetics of Iron sucrose injection have not been studied.

Distribution:
Following intravenous administration of iron sucrose, the iron component appears to distribute mainly in blood and to some extent in extravascular fluid. Significant amount of the administered iron distributes in the liver, spleen and bone marrow.

Metabolism and Elimination:
Following intravenous administration of Iron sucrose (Referis) is dissociated into iron and sucrose by the reticuloendothelial system. The sucrose component is eliminated mainly by urinary excretion.Some iron also is eliminated in the urine.

Indications :

For the treatment of Iron deficiency in the following indications:

- where there is a need for a rapid Iron supply,
- In patients who cannot tolerate oral iron therapy or who are non compliant,
- In active inflammatory bowel disease where oral iron preparations are ineffective,
- In chronic kidney disease when oral iron preparations are less effective.

Posology and method of administration:
Monitor carefully patients for signs and symptoms of hypersensitivity reactions during and following each administration of Iron Sucrose.
Iron Sucrose should only be administered when staff trained to evaluate and manage anaphylactic reactions is immediately available, in an environment where full resuscitation facilitates can be assured. The patient should be observed for adverse effects for at least 30 minutes following each Iron Sucrose injection.

Posology :
The cumulative dose of Iron Sucrose must be calculated for each patient individually and must not be exceeded.

Calculation of Dosage :
The total cumulative dose of Iron Sucrose, equivalent to the total Iron deficit (mg), is determined by the haemoglobin level (Hb) and body weight (BW).
The dose of Iron Sucrose must be individually calculated for each patient according to the total iron deficit calculated with the following Ganzoni formula, for example.
Total iron deficit [mg] = BW [kg] x (target Hb - actual Hb) [g/dl] x 2.4* + storage iron [mg]
- Below 35kg BW: Target Hb = 13 g/dl and storage iron = 15mg/kg BW
- 35kg BW and above: Target Hb = 15g/dl and storage iron = 500mg

* Factor 0.24 = 0.0034 (Iron content of Hb is equal to 0.34%) x 0.07 (Blood volume is equal to 7% of BW) x 1000 (conversion of (g) to (mg)) x 10

$$\text{Total Iron Sucrose to be administered (in mL)} = \frac{\text{Total iron deficit (mg)}}{\text{20 mg Iron mL}}$$

Total amount of Iron Sucrose (mL) to be administered according to body weight, actual Hb level and target Hb level*

Total amount of Iron Sucrose (20mg Iron per mL) to be administered				
Body Weight	Hb 6.0 g/L	Hb 7.5 g/L	Hb 9.0 g/L	Hb 10.5 g/L
30 kg	47.5 mL	42.5 mL	37.5 mL	32.5 mL
35 kg	62.5 mL	57.5 mL	50 mL	45 mL
40 kg	67.5 mL	60 mL	55 mL	47.5 mL
45 kg	75 mL	65 mL	57.5 mL	50 mL
50 kg	80 mL	70 mL	60 mL	52.5 mL
55 kg	85 mL	75 mL	65 mL	55 mL
60 kg	90 mL	80 mL	67.5 mL	57.5 mL
65 kg	95 mL	82.5 mL	72.5 mL	60 mL
70 kg	100 mL	87.5 mL	75 mL	62.5 mL
75 kg	105 mL	92.5 mL	80 mL	65 mL
80 kg	112.5 mL	97.5 mL	82.5 mL	67.5 mL
85 kg	117.5 mL	102.5 mL	85 mL	70 mL
90 kg	122.5 mL	107.5 mL	90 mL	72.5 mL

Below 35kg BW : Target Hb = 13 g/dl
35kg BW and above : Target Hb = 15g/dl
To convert Hb (mM) to Hb (g/dl), multiply the former by 1.6
If the total necessary dose exceeds the maximum allowed single dose, then the administration must be divided.

Posology :
Adults :
5-10mL of iron Sucrose (100 – 200 mg Iron) 1 to 3 times a week. For administration time and dilution ratio see "Method of Administration".

Paediatric population :
The use of Iron Sucrose has not been adequately studied in children and therefore, Iron Sucrose is not recommended for use in children.

Method of administration :
Iron Sucrose must only be administrated by the intravenous route. This may be by a slow intravenous injection, by an intravenous drip infusion or directly into the venous line of the dialysis machine.

Intravenous drip infusion :
Iron Sucrose must only be diluted in sterile 0.9% m/V sodium chloride (NaCl) solution. Dilution must take place immediately prior to infusion and the solution be administered as follows :

Iron Sucrose dose (mg of Iron)	Iron Sucrose dose (mL of Iron Sucrose)	Maximum dilution volume of sterile 0.9% m/V NaCl solution	Minimum infusion time
50 mg	2.5 mL	50 mL	8 minutes
100 mg	5 mL	100 mL	15 minutes
200 mg	10 mL	200 mL	30 minutes

For stability reasons dilutions to lower Iron Sucrose concentrations are not permissible.

Intravenous injection :
Iron Sucrose may be administered by slow intravenous injection at a rate of 1mL undiluted solution per minute and not exceeding 10 mL Iron Sucrose (200 mg Iron) per injection.

Injection into venous line of dialysis machine :
Iron Sucrose may be administered during a haemodialysis session directly into the venous line of the dialysis machine under the same conditions as for intravenous injection.

Note:
Do not mix Iron Sucrose Injection (Referis) with other medications or add to parenteral nutrition solutions for intravenous infusion. Parenteral drug products should be inspected for particulate matter and discoloration prior to administration, whenever the solution and container permit.

Undesirable effects :

System Organ class	Common (≥1/100,<1/10)	Uncommon (≥1/1,000,<1/100)	Rare (≥1/10,000<1/1,000)	Frequency not known
Infections and infestations			Pneumonia	
Blood and lymphatic system disorders		Polycythemia[2]		
Immune system disorders		Hypersensitivity		Anaphylactoid reactions, angioedema
Metabolism and nutrition disorders			Iron overload	
Nervous system disorders	Dysgeusia	Headache, dizziness, burning sensation, paraesthesia, hypoaesthesia	Syncope, migraine, somnolence	Depressed level of consciousness, confusional state, loss of consciousness, anxiety, tremor
Cardiac disorders			Palpitations	Bradycardia, tachycardia
Vascular disorders	Hypotension, hypertension	Phlebitis	Flushing	Circulatory collapse, superficial vein thrombosis, thrombophlebitis,
Respiratory disorders and mediastinal disorders		Dyspnoea		Bronchospasm
Renal and urinary disorders		Chromaturia		
Gastrointestinal disorders	Nausea	Vomiting , abdominal pain, diarrhoea, constipation	Dry mouth	
Skin and subcutaneous tissue disorders		Pruritus, rash		
Musculoskeletal and connective tissue disorders		Muscle cramps, myalgia, arthralgia, pain in extremity, back pain	Limb disobrt muscle spasms	Hypotonia
General disorders and administration site condition	Injection site pain	Chills, injection site reactions, injection site irritation, injection site discoloration, injection site burning, asthenia, fatigue, pain	Feeling hot, chest pain, pyrexia, injection site pruritus, injection site bruising	Hyperhidrosis
Investigations		Gamma-glutamyltransferase increased, alanine aminotransferase increased, aspartate aminotransferase increased, liver function test abnormal	Serum ferritin increased[2], blood creatinine increased, blood lactate dehydrogenase increased	

Warnings: Hypersentivity reactions have been reported with Injectable Iron products.

Precautions
General:
Because body iron excretion is limited and excess tissue iron can be hazardous, caution should be exercised to withhold iron administration in the presence of evidence of tissue iron overload. Patients receiving Iron sucrose require periodic monitoring of hematologic and hematinic parameters (haemoglobin, haematocrit, serum ferritin and transferrin saturation). Iron therapy should be withheld in patients with evidence of iron overload. Transferrin saturation values increase rapidly after IV administration of iron sucrose (Referis) injection; thus, serum iron values may be reliably obtained 48 hours after IV dosing

Hypersensitivity Reactions:
Serious hypersensitivity reactions have been reported including life threatening and fatal anaphylactic/anaphylactoid reactions in patients receiving Iron sucrose.

Hypotension:
Hypotension has been reported frequently in haemodialysis dependent chronic kidney disease patients receiving intravenous iron. Hypotension following administration of Iron sucrose (Referis) injection may be related to rate of administration and total dose administered. Caution should be taken to administer Iron sucrose according to recommended guidelines.

Carcinogenesis, Mutagenesis, and Impairment of Fertility:
No long-term studies in animals have been performed to evaluate the carcinogenic potential of Iron sucrose.
Iron sucrose (Referis) injection was not genotoxic in the Ames test, the mouse lymphoma cell (L5178Y/TK+/-) forward mutation test, the human lymphocyte chromosome aberration test, or the mouse micronucleus test.
Iron Sucrose Injection (Referis) injection at IV doses up to 15mg iron/kg/day (about 1.2 times the recommended maximum human dose on a body surface area basis) was found to have no effect on fertility and reproductive performance of male and female rats.

Pregnancy Category B:
There are, however, no adequate and well controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

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 (Referis) injection is administered to a nursing woman.

Paediatric Use:
Safety and effectiveness of Iron sucrose (Referis) injection in paediatric patients have not been established.

Geriatric Use:
No overall differences in safety were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

Caution:
Before using check for absence of sediments. The injection should be discarded if any visible particles appear.

Overdose:
Dosages of Iron Sucrose (Referis) injection in excess of iron needs may lead to accumulation of iron in storage sites leading to haemosiderosis. Periodic monitoring of iron parameters such as serum ferritin and transferring saturation may assist in recognizing iron accumulation. Iron Sucrose (Referis) injection should not be administered to Patients with iron overload and should be discontinued when serum ferritin levels equal or exceed established guidelines. Particular caution should be exercised to avoid iron overload where anemia unresponsive to treatment has been incorrectly diagnosed as iron deficiency anemia.

Symptoms associated with over dosage or infusing Iron sucrose (Referis) injection too rapidly included hypotension, headache, vomiting, nausea, dizziness, joint aches, paraesthesia, abdominal and muscle pain, edema, and cardiovascular collapse. Most symptoms have been successfully treated with IV fluids, hydrocortisone, and/or antihistamines. Infusing the solution as recommended or at a slower rate may also alleviate symptoms.

Contraindications:
The use of Iron Sucrose (Referis) injection is contraindicated in patients with evidence of iron overload or hereditary disturbances in utilization of iron, in patients with known hypersensitivity to Iron Sucrose (Referis) injection or any of its inactive compounds and in patients with anemia not caused by iron deficiency, known serious hypersensitivity to other parenteral iron products.

Caution: Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

Availability :
Pack of 5 ampoules in a tray

Storage:
Store at temperatures not exceeding 30°C.
Keep out of reach of children.

Manufactured by:
Maiva Pharma Private Limited
No.32, Sipcot Industrial Complex,
Phase 1, Hosur-635126, Tamil Nadu, INDIA.

Imported & Distributed by:
Biocare Lifesciences, Inc.
4th Floor, 393 Goodwill Bldg., Senator
Gil Puyat Ave., Brgy. Bel-Air, Makati City