1.8 The Summary of Product Characteristic

1. Name of the medicinal product

Ferobsv, Iron Sucrose Injection USP 100 mg/5 mL solution for injection or concentrate for solution for infusion.

2. Qualitative and Quantitative Composition

One milliliter of solution contains 20 mg of iron as iron sucrose (iron (III)-hydroxide sucrose complex).

Each 5 ml ampoule of Iron Sucrose Injection contains Ferric Hydroxide in Complex with Sucrose equivalent to Elemental Iron 100 mg.

Water for Injections Ph.Eur q.s. to 5 mL.

3. Pharmaceutical Form

Solution for injection or concentrate for solution for infusion

Iron Sucrose Injection is a brown, non transparent, aqueous solution.

4. Clinical Particulars

4.1 Therapeutic Indications

Iron Sucrose Injection is indicated for the treatment of iron deficiency in the following indications:

- Where there is a clinical need to deliver iron rapidly to iron stores,
- In patients who cannot tolerate oral iron therapy or who are non-compliant,
- In active inflammatory bowel disease where oral iron preparations are ineffective.

The diagnosis of iron deficiency must be based on appropriate laboratory tests (e.g. Hb, serum ferritin, serum iron, etc.).

4.2 Posology and Method of Administration

Administration: Iron Sucrose Injection must only be administered by the intravenous route. This may be by a slow intravenous injection or by an intravenous drip infusion. Before administering the first dose to a new patient, a test dose of Iron Sucrose Injection should be given.

Iron Sucrose Injection must not be used for Intramuscular injection.

Adults and the Elderly:

The total cumulative dose of Iron Sucrose Injection, equivalent to the total iron deficit (mg), is determined by the haemoglobin level and body weight. The dose for Iron Sucrose Injection 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 = 130 g/l and depot iron = 15 mg/kg body weight

• 35 kg body weight and above: target Hb = 150 g/l and depot iron = 500 mg

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

The total amount of Iron Sucrose Injection required in mg is determined from above calculation.

Alternatively, the total amount of Iron Sucrose Injection required in ml is determined from the following formula or dosage table.

$$\text{Total amount of Iron Sucrose Injection required [ml]} = \frac{\text{Total iron deficit [mg]}}{20\ \text{mg/ml}}$$

Dosage table stating the total amount of		**Iron Sucrose Injection in ml**	**:**

Body Weight	Total amount of Iron Sucrose Injection to be administered			
	Hb 60 g/l	Hb 75 g/l	Hb 90 g/l	Hb 105 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

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

Example: For a patient of 60 kg body weight with an actual Hb of 60 g/l 90 ml should be administered. (Alternatively 18 ampoules/vials of 5 ml or 36 vials of 2.5 ml should be administered).
Dosage: The total single dose must not exceed 200 mg of iron given not more than three times per week. If the total necessary dose exceeds the maximum allowed single dose, then the administration has to be split.
Children: The use of Iron Sucrose Injection has not been adequately studied in children and, therefore, Iron Sucrose Injection is not recommended for use in children.
Intravenous drip infusion: Iron Sucrose Injection must be diluted only in sterile 0.9% m/V sodium chloride solution:
• 2.5 ml Iron Sucrose Injection (50 mg iron)
in max. 50 ml sterile 0.9% m/V sodium chloride solution
• 5 ml Iron Sucrose Injection (100 mg iron)
in max. 100 ml sterile 0.9% m/V sodium chloride solution

• 10 ml Iron Sucrose Injection (200 mg iron)
in max. 200 ml sterile 0.9% m/V sodium chloride solution
For stability reasons, dilutions to lower Iron Sucrose Injection concentrations are not permissible.
Dilution must take place immediately prior to infusion and the solution should be administered as follows:
• 100 mg iron (5 ml Iron Sucrose Injection) in at least 15 minutes
• 200 mg iron (10 ml Iron Sucrose Injection) in at least 30 minutes
The first 25 mg of iron (i.e. 25 ml 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 50 ml in 15 minutes.
Intravenous injection: Iron Sucrose Injection may be administered by slow intravenous injection at a rate of 1 ml undiluted solution per minute and not exceeding 10 ml Iron Sucrose Injection (200 mg iron) per injection.
Before administering a slow intravenous injection, a test dose of 1 ml (20 mg 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: Iron Sucrose Injection may be administered during a haemodialysis session directly into the venous limb of the dialyser under the same procedures as those outlined for intravenous injection.

4.3 Contraindications

The use of Iron Sucrose Injection is contraindicated in cases of:
• known hypersensitivity to Iron Sucrose Injection or any of its excipients
• anaemias not attributable to iron deficiency
• iron overload or disturbances in utilisation 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.

4.4 Special Warnings and Precautions for use

Parenterally 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 bacteraemia. 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 Injection at the injection site may lead to pain, inflammation, tissue necrosis and brown discoloration of the skin.

4.5 Interaction with other medicinal products and other forms of interaction

As with all parenteral iron preparations, Iron Sucrose Injection 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 Injection.

4.6. Pregnancy and Lactation

Data on a limited number of exposed pregnancies indicated no adverse effects of Iron Sucrose Injection on pregnancy or on the health of the foetus/newborn child. No well-controlled studies in pregnant women are available to date. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development.
Nevertheless, risk/benefit evaluation is required.
Iron Sucrose Injection should only be used in pregnant women in whom oral iron is ineffective or cannot be tolerated and the level of anaemia is judged sufficient to put the mother or foetus at risk.
Pregnancy first trimester: see contraindications.
Non metabolised Iron Sucrose Injection is unlikely to pass into the mother's milk. No well-controlled clinical studies are available to date. Animal studies do not indicate direct or indirect harmful effects to the nursing child.

4.7 Effects on ability to drive and use machines

In the case of symptoms of dizziness, confusion or light headedness following the administration of Iron Sucrose Injection, patients should not drive or use machinery until the symptoms have ceased.

4.8 Undesirable Effects

The most frequently reported adverse drug reactions (ADRs) of Iron Sucrose Injection in clinical trials were transient taste perversion, hypotension, fever and shivering, injection site reactions and nausea, occurring in 0.5 to 1.5% of the patients. Non-serious anaphylactoid reactions occurred rarely.
In general anaphylactoid reactions are potentially the most serious adverse reactions (see "Special warnings and Precautions for Use" section 4.4).
In clinical trials, the following adverse drug reactions have been reported in temporal relationship with the administration of Iron Sucrose Injection, with at least a possible causal relationship:

Nervous system disorders
Common (≥ 1/100, < 1/10): transient taste perversions (in particular metallic taste).
Uncommon (≥ 1/1000, < 1/100): headache, dizziness.
Rare (≥ 1/10000, < 1/1000): paraesthesia, syncope, loss of consciousness, burning sensation.

Cardio-vascular disorders
Uncommon (≥ 1/1000, < 1/100): hypotension and collapse, tachycardia and palpitations.
Rare (≥ 1/10000, < 1/1000): hypertension.

Respiratory, thoracic and mediastinal disorders
Uncommon (≥ 1/1000, < 1/100): bronchospasm, dyspnoea.

Gastrointestinal disorders
Uncommon (≥ 1/1000, < 1/100): nausea; vomiting, abdominal pain, diarrhoea.

Skin and subcutaneous tissue disorders
Uncommon (≥ 1/1000, < 1/100): pruritus, urticaria, rash, exanthema, erythema.

Musculoskeletal, connective tissue and bone disorders
Uncommon (≥ 1/1000, < 1/100): muscle cramps, myalgia.

General disorders and administration site disorders
Uncommon (≥ 1/1000, < 1/100): fever, shivering, flushing, chest pain and tightness. Injection site disorders such as superficial phlebitis, burning, swelling.
Rare (≥ 1/10000, < 1/1000): arthralgia, peripheral oedema, fatigue, asthenia, malaise, feeling hot, oedema.

Immune system disorders

Rare (≥ 1/10000, < 1/1000): anaphylactoid reactions.
Moreover, in spontaneous reports the following adverse reactions have been reported:
Isolated cases: reduced level of consciousness, light-headed feeling, confusion, angio-oedema, swelling of joints, hyperhidrosis, back pain, bradycardia, chromaturia.

4.9 Overdose

Overdosage can cause acute iron overloading which may manifest itself as haemosiderosis. Overdosage should be treated, if required, with an iron chelating agent.

5. Pharmacological properties

5.1 Pharmacodynamic properties

The ferrokinetics of Iron Sucrose Injection labelled with 59Fe and 52Fe were assessed in 5 patients with anaemia and chronic renal failure. Plasma clearance of 52Fe was in the range of 60 to 100 minutes. 52Fe was distributed to the liver, spleen and bone marrow. At two weeks after administration, the maximum red blood cell utilisation of 59Fe ranged from 62% to 97%.

5.2 Pharmacokinetic properties

Following intravenous injection of a single dose of Iron Sucrose Injection containing 100 mg iron in healthy volunteers, maximum iron levels, averaging 538 µmol/l, were obtained 10 minutes after injection. The volume of distribution of the central compartment corresponded well to the volume of plasma (approximately 3 litres).

The iron injected was rapidly cleared from the plasma, the terminal half-life being approx. 6 h. The volume of distribution at steady state was about 8 litres, indicating a low iron distribution in the body fluid. Due to the lower stability of iron sucrose in comparison to transferrin, a competitive exchange of iron to transferrin was observed. This resulted in iron transport of approx. 31 mg iron/24 h.

Renal elimination of iron, occurring in the first 4 h after injection, corresponds to less than 5% of the total body clearance. After 24 h the plasma levels of iron were reduced to the pre-dose iron level and about 75% of the dosage of sucrose was excreted.

5.3 Preclinical Safety Data

There are no preclinical data of relevance to the prescriber that are additional to information already in other sections of the SPC.

6. Pharmaceutical particulars

6.1 List of Excipients

Sodium hydroxide

Water for Injections

6.2 Incompatibilities

Iron Sucrose Injection must only be mixed with sterile 0.9% m/V Sodium chloride solution. No other solutions and therapeutic agents should be used as there is the potential for precipitation and/or interaction. The compatibility with containers other than glass, polyethylene and PVC is not known.

6.3 Shelf Life

24 Months from the date of manufacturing.

Before using check the absence of sediments. The Injection should be discarded if any visible particles appear.

6.4 Special precautions for storage

Store at a temperature below 30 ^{0}C.

Do not Freeze. Keep out of reach of Children.

6.5 Nature and contents of container

Iron Sucrose Injection is available in 5 mL single use ampoule in a Tray.

Pack of 5 ampoules in a tray along with package insert, packed in a printed outer carton.

6.6 Special precautions for disposal and other handling

Ampoules or vials should be visually inspected for sediment and damage before use. Only those with sediment free and homogenous solution must be used.

The diluted solution must appear as brown and clear.

Each ampoule of Iron Sucrose Injection is intended for single use only. Discard any remaining contents after first use.

7. Marketing Authorization Holder

Global Pharmatech Private Limited,
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Phase-I,
Hosur- 635126
Tamil Nadu - INDIA
Website: http://www.globalpharmatech.com

8. Marketing Authorization number(s)

New Registration

9. Date of First Authorization/Renewal of the Authorization

New Registration

10. Date of Revision of the text

Not Applicable