134mm x 203mm

FRONT

℞

IRON

IRSUC

20 mg/mL (100 mg / 5 mL) Solution for Injection (IV)

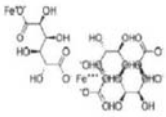
HEMATINIC

FORMULATION/COMPOSITION:

Each mL contains:
Ferric Hydroxide in Complex with
Sucrose equivalent to elemental Iron . . . . . 20 mg
Water for Injection BP . . . q.s.

DESCRIPTION:

Iron (as Ferric Hydroxide Sucrose Complex) is a sterile, dark brown slightly viscous solution of ferric hydroxide in complex with Sucrose in Water for Injection filled in a 5 ml amber coloured glass ampoule containing Ferric Hydroxide in complex with Sucrose as its active ingredient. Its chemical name is (2R,3R,4S,5S,6R)-2-[(2S,3S,4S,5R)-3,4-dihydroxy-2,5-bis(hydroxymethyl) oxolan-2-yl]oxy-6(hydroxymethyl)oxane-3,4,5-tri.iron(3+); Oxygen (2-). It has a molecular weight of 34,000 to 64,000 daltons and its molecular formula is [Na2Fe5O8(OH)·3(H2O)]n· m(C12H22O11). The structural formula is :



PHARMACODYNAMIC PROPERTIES:

Following intravenous administration of Iron (as Ferric Hydroxide Sucrose Complex) is dissociated by the endothelial system into iron and sucrose. In 22 hemodialysis patients on erythropoietin (recombinant human erythropoietin) therapy treated with iron sucrose containing 100 mg iron, three times weekly for three weeks, significant increases in serum iron and serum ferritin and significant decreases in total iron binding capacity occured four weeks from the initiation of iron sucrose treatment.

PHARMACOKENETIC PROPERTIES:

Following intravenous injection of a single dose of iron sucrose injection USP containing 100 mg iron in healthy volunteers, maximum iron levels, averaging 538 Mmol/L, were obtained 10 minutes after injection. The volume of distribution of 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. 6h. 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 result in iron transport of approx. 31 mg iron/24h.
Renal elimination of iron, occuring in the first 4h after injection, corresponds to less than 5% of the total body clearance. After 24h the plasma levels of iron were reduced to the pre-dose iron level and about 75% of the dosage of sucrose was excreted.

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 administered iron is distributed in the liver, spleen and bone marrow.
METABOLISM AND ELIMINATION:
Following intravenous administration, iron sucrose dissociated into iron and sucrose by the reticuloendothelial system. The sucrose component is eliminated mainly by urinary excretion.

ADVERSE DRUG REACTION:

The most frequently reported adverse drug reaction (ADRc) of Iron Sucrose in clinical trails were transient tast perversion, hypotension, fever and shivering, injection site reaction and nausea, occuring in 0.5 to 105% of the patients. Non-serious anaphylactoid reactions occurred rarely. In general anaphylactoid reactions are potentially the most serious adverse reaction.

INDICATIONS:

For the treatment of iron deficiency in the following indications.
- Where there is a clinical 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.

Iron sucrose Injection USP is indicated for the treatment of iron
deficiency in the following indications:
Pre existing (moderate to severe) anemia
Patients not responding or having poor compliance with oral iron supplements
Pre and postoperative period
Postpartum anemia and postpartum haemorrhage
Patients with poor iron absorption (bowel operations or diseases)
Patients with severe renal impairment
Treatment of Iron Deficiency Anemia in the following patients: Hemodialysis Dependent Chronic Kidney Disease (HDD-CKD) patients receiving an Erythropoietin.
Peritoneal Dialysis Dependent Chronic Kidney Disease (PDD-CKD) patients receiving an Erythropoietin.
Non-Dialysis Dependent Chronic Kidney Disease (NDD-CKD) patients receiving or not receiving an Erythropoietin.
During Pregnancy and Post partum.

DOSAGE AND MODE/ROUTE 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 facilities can be assured. The patient should be observer for adverse effects for at least 30 minutes following each Iron Sucrose Injection (see section 4.4).

Dosage:

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 35 kg BW: Target Hb = 13 g/dl and storage iron = 15 mg/kg BW
- 35 kg BW and Target Hb = 15 g/dl and storage iron = 500 mg

above: * Factor 2.4 = 0.0034 (iron content of Hb = 0.34%) x 0.07 (blood volume = 7% of BW) x 1000 (conversion of [g] to [mg]) x 10

Total Iron Injection 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*:

BW	Total amount of Iron Sucrose (20 mg iron per ml) to be administered			
	Hb 6.0 g/dl	Hb 7.5 g/dl	Hb 9.0 g/dl	Hb 10.5 g/dl
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 35 kg BW: Target Hb = 13 g/dl
35 kg BW and above: Target Hb = 15 g/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.

Dosage

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

Pediatric 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 administered 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 should 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 1 mL 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.

CONTRAINDICATION:

The use of Iron (as Ferric Hydroxide Sucrose Complex) is contraindicated in the following conditions: Hypersensitivity to the active substance, to Iron Sucrose or any of its excipients.
Known serious hypersensitivity to other parenteral iron products. Anaemia not caused by iron deficiency.
Evidence of iron overload or hereditary disturbances in utilisation of iron.
The use of iron sucrose is contraindicated in patients with evidence of iron overload, in patients with known hypersensitivity to it or any of its inactive components, and in patients with anemia not caused by iron deficiency.

134mm x 203mm

BACK

SPECIAL WARNINGS AND PRECAUTIONS:

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 including iron sucrose. There have been reports of hypersensitivity reactions which progressed to Kounis syndrome (acute allergic coronary arteiospasm that can result in myocardial infarction, see section Undesirable Effects). In several studies performed in patients who had a history of a hypersensitivity reaction to iron dextran or ferric gluconate, IRSUC was shown to be well tolerated. For known serious hypersensitivity to other parenteral iron product see section Contraindications. The risk of hypersensitivity reactions 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 conditions (e.g. systemic lupus erythermatosus, rheumatoid arthritis). Iron Injection 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. Each patient should be observed for adverse effects for at least 30 minutes following each Iron injection. 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. 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 prescipitating factor, in particular Porphyria Cutanea Tarda (PCT). Careful monitoring of iron status is recommended to avoid iron overload. Parenteral iron should be used with caution in the case of acute or chronic infection. It is recommended that the administration of Iron Injection is stopped in patients with bacteraemia. In patients with chronic infection, a risk/benefit evaluation should be performed. Paravenous leakage must be avoided because leakage of Iron Injection at the injection site can lead to pain, inflammation and brown discoloration of the skin. Iron Injection contains up to 7 mg sodium per mL, equivalent to 0.4% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

Warnings:

Hypersensitivity reactions have been reported with injectable iron products.

Special 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 requires periodic monitoring of hematologic and hematinic parameters. Iron therapy should be withheld in patients with evidence of iron overload. Transferrin saturation values increase rapidly after IV administration of iron sucrose; thus serum iron values may be reliably obtained 48 hrs after IV dosing.

Hypersensitivity Reactions: Serious hypersensitivity reactions have been rarely reported in patients receiving iron sucrose.

Hypotension: Hypotension has been reported in chronic kidney disease patients receiving intravenous iron. Hypotension following administration of iron sucrose 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. Use in Pregnancy: Pregnancy Category B. No adequate and well controlled studies in pregnant women have been reported. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Use in Lactation: It is not known whether this drug is excreted in human milk. Caution should be exercised when iron sucrose is administered to a nursing woman.

Use in Children: Safety and effectiveness of iron sucrose in pediatric patients have not been established.

Use in Elderly: There are no identified differences in responses between elderly and younger patients, but greater sensitivity of some of the older individuals cannot be ruled out.

INTERACTION WITH OTHER MEDICAMENTS:

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

PREGNANCY AND LACTATION:

Data on limited number of exposed pregnancies indicated no adverse effects of Iron Sucrose Injection USP 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 USP 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.

Non metabolised Iron sucrose Injection USP 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.

UNDESIRABLE EFFECTS:

The most commonly reported adverse drug reaction in clinical trials with Iron Sucrose was dysgeusia, which occured with a rate of 4.5 events per 100 subjects. The most important serious adverse drug reactions associated with Iron Sucrose are hypersensitivity reactions, which occured with a rate of 0.25 events per 100 subjects in clinical trials.

The adverse drug reactions reported after the administration of Iron Sucrose in 4,046 subjects in clinical trials as well as those reported from the post-marketing setting are presented in the table below.

System Organ Class	Common: (≥1/100, <1/10)	Uncommon: (≥ 1/100, <1/10)	Rare (≥1/10,000, <1/1,000)	Frequency not known[1]
Infections and Infestations			Pneumonia	
Blood and lymphatic system disorders		Polycythemia[2]		
Immune system disorders		Hypersensitivity		Anaphylactoid reactions, angiodema
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
Respiratory thoracic and mediastinal disorders		Dsypnoea		Bronchospasm
Renal and urinary disorders		Chromaturia		
Gastrointestinal disorders	Nausea	Vomiting, abdominal pain, diarrhoea, conspitation	Dry mouth	
Skin and subcutaneous tissue disorders		Pruritus, rash		Urticaria, erythema
Musculoskeletal and connective tisue disorders		Muscle cramps, myalgia, arthragia, pain in extremity, back pain	Limb discomfort, muscle spasms	Hypotonia
General disorders and administration site conditions	Injection site pain	Chills, injection site reactions, injection site irritation, injection site extravasation, injection site discoloration, injection site burning, asthenia, fatigue, pain	Feeling hot, chest pain, pyrexia, injection site pruritus, injection site bruising.	Hyperhidrosis, cold sweat, malaise, pallor
Investagations		Gamma glutamytransferase increased, alanine aminotransferase increased, aspartate aminotransferase increased, liver function tests abnormal	Serrum ferritin increased[2], blood creatinine increased, blood lactate dehydrogenase increased	

1.) Spotaneous reports from the post marketing setting.
2.) Possibly as consequence of iron overdose or iron overload

SIDE EFFECTS:

Side effects include hypotension, chest pain, hypervolemia, CHF, cramps, musculoskeletal pain, diarrhea, nausea, vomiting, abdominal pain, elevated liver enzymes, skin irritation, pruritis, application site reaction, dizziness, dyspnea, pneumonia, cough, headache, fever, asthenia, malaise.

OVERDOSAGE AND TREATMENT:

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

Dosages of iron sucrose in excess of iron needs may lead to accumulation of iron in storage sites leading to hemosiderosis. Periodic monitoring of iron parameters such as serum ferritin and transferrin saturation may assist in recognizing iron accumulation. Iron sucrose 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 diagnoses as iron deficiency anemia.

STORAGE CONDITION:

Store at temperature not exceeding 30°C. Protect from light. Do not freeze.

SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING

Ampoules or vials should be visually inspected for sediment and damage before use. Use only those containing a sediment free and homogenous solution. Iron Injection must not be mixed with other medicinal products except sterile 0.9% m/V sodium chloride solution for dilution. For instructions on dilution of the product before administration, see section Dosage and Mode/Route of Administration. The diluted solution must appear as brown and clear.

Each ampoule of IRSUC is intended for single use only.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

KEEP OUT OF REACH OF CHILDREN
For single use only

CAUTION:

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

For suspected adverse drug reaction, report to the FDA:www.fda.gov.ph.

Patients are advised to seek medical attention immediately at the first sign of any adverse drug reaction.

AVAILABILITY:

5 mL USP Type I Amber Glass Ampoule (Box of 5 Ampoules in a Plastic Tray)

- FDA Registration No.: DRP-7111-08
- Date of First Authorization / Renewal of authorization: 10 May 2022
- Date of revision of Package Insert: May 2022

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