Artwork Code : 1400007778	**Artwork Req. No: 26489**
Quality of Paper/Board : Super Sun Shine	**Size of Artwork (In mm) : 400x175**
Quality of Gum :	**GSM of Paper/Board : 60 GSM**

Colour Code : BLACK ■ | Pantone ☐ | Pantone ☐ | Pantone ☐ | Pantone ☐ | Pantone ☐ | Pantone ☐ | Pantone ☐

Barcode Information:	
Barcode Scan Report:	
Packing: 5ml Molded vial	**Plant Location : Injectable**
Country: Malaysia	**Language : English**
Ref. Code Creation/Blockage Note:	**Artwork Control Key No.:**

"Controlled Copy" Holder (1) (2) (3) (4) (5)

Date: 23/09/22

Baxter

For the use of registered medical practitioner, hospital or laboratory use

SUCROFER™

Iron Sucrose Injection USP (20 mg/ml)

Name of the medicinal product
Iron Sucrose Injection USP (20 mg/ml) Sucrofer

Qualitative and quantitative composition
Each ml Contains:
Ferric Hydroxide in Complex with Sucrose
equivalent to elemental iron 20 mg
Water for Injection USP q.s.

Pharmaceutical form
Solution for injection or concentrate for solution for infusion.
Iron Sucrose Injection USP (20 mg/ml) – Sucrofer, is Dark brown viscous aqueous solution.

Pharmacological properties
Pharmacodynamic properties
Pharmacotherapeutic group: Anti-anaemic preparation, iron, parenteral preparation, ATC code: B03AC
Mechanism of action
Iron sucrose, the active ingredient of Sucrofer, is composed of a polynuclear iron (III)-hydroxide core surrounded by a large number of non-covalently bound sucrose molecules. The complex has a weight average molecular weight (Mw) of approximately 43kDa. The polynuclear iron core has a structure similar to that of the core of the physiological iron storage protein ferritin. The complex is designed to provide, in a controlled manner, utilisable iron for the iron transport and storage proteins in the body (i.e., transferrin and ferritin, respectively).
Following intravenous administration, the polynuclear iron core from the complex is taken up predominantly by the reticuloendothelial system in the liver, spleen, and bone marrow.
In a second step, the iron is used for the synthesis of Hb, myoglobin and other iron-containing enzymes, or stored primarily in the liver in the form of ferritin.

Pharmacokinetic properties
Distribution
The volume of distribution of the central compartment corresponded well to the volume of plasma (approximately 3 litres).
Biotransformation
Upon injection, sucrose largely dissociates and the polynuclear iron core is mainly taken up by the reticuloendothelial system of the liver, spleen, and bone marrow. At 4 weeks after administration, red cell iron utilization ranged from 59 to 97%.
Elimination
The iron sucrose complex has a weight average molecular weight (Mw) of approximately 43 kDa, which is sufficiently large to prevent renal elimination. Renal elimination of iron, occurring in the first 4 h after injection of a Sucrofer dose of 100 mg iron, corresponds to less than 5% of the dose. After 24 h the total serum iron concentration was reduced to the pre-dose iron level. Renal elimination of sucrose was about 75% of the Administered dose

Therapeutic indications
Sucrofer is indicated 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.
- Where oral iron preparations are in-effective. (e. g., in active inflammatory bowel disease)

Sucrofer should only be administered where the indication is confirmed by appropriate investigations.

Posology and method of administration
Posology
The cumulative dose of Sucrofer must be calculated for each patient individually and must not be exceeded.
Calculation of dosage
The total cumulative dose of Sucrofer, equivalent to the total iron deficit (mg), is determined by the haemoglobin level (Hb) and body weight(BW). The dose of Sucrofer 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 above:
Target Hb = 15 g/dl and storage iron = 500 mg
* 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 Sucrofer to be administered (in ml)

$$= \frac{\text{Total iron deficit [mg]}}{\text{20 mg iron /ml}}$$

Total amount of Sucrofer (ml) to be administered according to body weight, actual Hb level and target Hb level*:

BW	Total number of vial Sucrofer (20 mg iron per ml) to be administered:(1 vial of Sucrofer corresponds to 5 ml)			
	Hb 6.0 g/dl	Hb 7.5 g/dl	Hb 9.0 g/dl	Hb 10.5 g/dl
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

* 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/l), multiply the former by 1.6
If the total necessary dose exceeds the maximum allowed single dose, then the administration must be divided.

Calculation of dosage for iron replacement secondary to blood loss and to support autologous blood donation
The required Sucrofer dose to compensate for the iron deficit may be calculated according the following formulas:
If the quantity of blood lost is known: The administration of 200 mg iron (10 ml of Sucrofer) should result in an increase in Hb approximately equivalent to 1 unit blood (400 ml with Hb = 15 g/dl).
Iron to be replaced [mg] = Number of blood units lost x 200 mg or
Amount of Sucrofer needed [ml] = Number of blood units lost x 10 ml
If the Hb level is less than desired: Formula assumes that the storage iron does not need to be restored. Iron to be replaced [mg] = BW [kg] x 2.4 (target Hb – actual Hb) [g/dl]

Example: For BW = 60 kg and Hb decrease = 1 g/dl
⇒≅150 mg iron to be replaced
⇒7.5 ml Sucrofer needed
For the maximum tolerated single and weekly dose, see "Normal posology" and "Maximum tolerated single and weekly doses".

Normal posology:
Adults
5–10 ml of Sucrofer (100–200 mg iron) 1 to 3 times a week. For administration time and dilution ratio see "Method of administration".
Paediatric population
There is a moderate amount of data in children under study conditions. If there is a clinical need, it is recommended not to exceed 0.15 ml of Sucrofer (3 mg iron) per kg body weight not more than three times per week.
For administration time and dilution ratio see "Method of administration".

Maximum tolerated single and weekly doses
Adults
As an injection, maximum tolerated dose per day given not more than 3 times per week:
- 10 ml of Sucrofer (200 mg iron) injected over at least 10 minutes

As an infusion, maximum tolerated dose per day given not more than once per week:
- Patients above 70 kg body weight: 500 mg iron (25 ml of Sucrofer) over at least 3½ hours
- Patients of 70 kg body weight and below: 7 mg iron/kg body weight over at least 3½ hours

The infusion times given in "Method of administration" should be strictly adhered to, even if the patient does not receive the maximum tolerated single dose.
Method of administration
Sucrofer must only be administered by the intravenous route.
This may be by drip infusion, slow injection or directly into the venous line of the dialysis machine.
Intravenous drip infusion
Sucrofer 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:

Sucrofer dose (mg of iron)	Sucrofer dose (ml of Sucrofer)	Maximum dilution volume of sterile 0.9% m/V NaCl solution	Minimum Infusion Time
100 mg	5 ml	100 ml	15 minutes
200 mg	10 ml	200 ml	30 minutes
300 mg	15 ml	300 ml	1.5 hours
400 mg	20 ml	400 ml	2.5 hours
500 mg	25 ml	500 ml	3.5 hours

For stability reasons, dilutions to lower iron concentrations are not permissible.
Intravenous injection
Sucrofer may be administered by slow intravenous injection at a rate of 1 ml undiluted solution per minute and not exceeding 10 ml (200 mg iron) per injection.
Injection into venous line of dialysis machine
Sucrofer may be administered during a haemodialysis session directly into the venous line of the dialysis machine under the same conditions as for intravenous injection.

Route of Administration
Intravenous Injection

Contraindication
The use of Sucrofer is contraindicated in the following conditions:
- Hypersensitivity to the Active substance, to Sucrofer or any of its excipients
- Anaemias not caused by iron deficiency
- Evidence of Iron overload or hereditary disturbances in utilization of iron

Special warnings and precautions for use
Parenterally administered iron preparations can cause allergic or anaphylactoid reactions, which can be potentially fatal. Therefore,

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Date: 23/09/22

anti-allergic treatment should be available along with cardio-pulmonary resuscitation facilities and procedures. Hypersensitivity reactions have also been reported after previously uneventful doses of parenteral iron complexes including iron sucrose. Each patient should be observed for adverse effects for at least 30 minutes following each Sucrofer injection. There have been reports of hypersensitivity reactions which progressed to Kounis syndrome (acute allergic coronary arteriospam that can result in myocardial infarction, see section Undesirable effects).
In patients with a history of asthma, eczema, other atopic allergies or allergic reactions to other parenteral iron preparations, Sucrofer should be administered with caution as these patients may be particularly at risk of an allergic reaction. However, in several studies performed in patients who had a history of a hypersensitivity reaction to iron dextran or ferric gluconate, Sucrofer was shown to be well tolerated.
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. 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 Sucrofer 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 Sucrofer at the injection site can lead to pain, inflammation tissue necrosis and brown discoloration of the skin.

Interactions with other medicinal products and other forms of interaction
As with all parenteral iron preparations, it is recommended that Sucrofer is not administered concomitantly with oral iron preparations since the absorption of oral iron may be reduced.

Effects on ability to drive and use machines
Sucrofer is unlikely to influence the ability to drive or use machines. However, if symptoms such as dizziness, confusion or light-headedness occur following the administration of Sucrofer, affected patients should not drive a car or us machines until the symptoms have abated.

Fertility, pregnancy and lactation
Pregnancy
Sucrofer should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus, particularly during the first trimester (see section Special warnings and precautions for use).
Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity
Breastfeeding
There is limited information on the excretion of iron in human milk following administration of intravenous iron sucrose.
Preclinical data do not indicate direct or indirect harmful effects to the nursing child.
Fertility
No effects of iron sucrose treatment were observed on fertility, mating performance and early embryonic development in rats.

Undesirable effects
The adverse drug reactions reported after the administration of Iron Sucrose Injection those reported from the post-marketing setting are presented in the table below.

System Organ Class	Common (≥1/100, <1/10)	Uncommon (≥1/1,000, <1/100)	Rare (≥1/10,000,<1/1000)	Frequency not known[1])
Immune system disorders		Hypersensitivity		Angioedema, anaphylactoid /anaphylactic reactions
Nervous system disorders	Dysgeusia	Headache, dizziness, paraesthesia, hypoaesthesia	Syncope, somnolence	Depressed level of consciousness, confusional state, loss of consciousness, anxiety, tremor
Cardiac disorders			Palpitations	Bradycardia, tachycardia, Kounis syndrome
Vascular disorders	Hypotension, hypertension	Flushing, phlebitis		Circulatory collapse, thrombophlebitis
Respiratory, thoracic, and mediastinal disorders		Dyspnoea		Bronchospasm
Renal and urinary disorders			Chromaturia	
Gastrointestinal disorders	Nausea	Vomiting, abdominal pain, diarrhoea, constipation		
Skin and subcutaneous tissue disorders		Pruritus, rash		Urticaria, erythema
Musculoskeletal and connective tissue disorders		Muscle spasms, myalgia, arthralgia, pain in extremity, back pain		
General disorders and administration site conditions	Injection/ infusion site reactions[2])	Chills, asthenia, fatigue, oedema peripheral, pain	Chest pain, hyperhidrosis, pyrexia	cold sweat, malaise, pallor, influenza like illness[3])
Investigations		Alanine aminotransferase increased, aspartate aminotransferase increased, gamma glutamyltransferase increase, serum ferritin increased	Blood lactate dehydrogenase increased	

1) Spontaneous reports from the post-marketing setting estimated as rare
2) The most frequently reported are: injection/infusion site pain, extravasation, irritation reaction, discolouration, haematoma, pruritus
3) Onset may vary from a few hours to several days.

Overdose
Overdose can cause iron overload which may manifest itself as haemosiderosis. Overdose should be treated, as deemed necessary by the treating physician, with an iron chelating agent or according to standard medical practice.

List of excipients
Water for injection
Sodium hydroxide (for pH adjustment)

Incompatibilities
This medicinal product must not be mixed with other medicinal products except those mentioned in section Special precautions for disposal and other handling. There is the potential for precipitation and/or interaction if mixed with other solutions or medicinal products. The compatibility with containers other than glass, polyethylene and PVC is not known.

Shelf Life
18 months from the date of manufacturing.
Shelf life after first opening of the container:
From a microbiological point of view, the product should be used immediately.
Shelf life after dilution with sterile 0.9% m/V sodium chloride solution:
Chemical and physical in-use stability has been demonstrated for 7 days at 25 °C ± 2 °C, however from a microbiological point of view, the product should be used immediately after dilution If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 7 days at 25 °C ± 2 °C.

Storage Condition
Store Below 30°C. Do not freeze

Nature and contents of container
Iron Sucrose Injection USP (20mg/ml) - Sucrofer is available in 5 ml Glass Vial.

5's Pack: 5 Vials packed in 1 carton with Pack Insert.
10's Pack: 10 Vials packed in 1 carton with Pack Insert.

Special precautions for disposal and other handling
Vial should be visually inspected for sediment and damage before use. Use only those containing a sediment-free and homogenous solution.
Sucrofer 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 Posology and method of administration.
Each Vial of Sucrofer is intended for single use only.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements
"Controlled Medicine/Ubat Terkawal"
Date of Revision
September 2022

Product Registration Holder:
Baxter Healthcare (Malaysia) Sdn. Bhd.
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47301 Petaling Jaya, Selangor, Malaysia.

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