1.3.1 Summary of Product Characteristics (SmPC)

SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the medicinal Product

MARCFER (Iron Sucrose Injection BP)

2. Qualitative and Quantitative composition

Each ml contains:

Ferric Hydroxide in complex with sucrose

eq. to elemental iron 20mg

Water for Injection BP q.s.

3. Pharmaceutical form

Injection

4. Clinical Particulars

4.1 Therapeutic Indications

MARCFER 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

Monitor carefully patients for signs and symptoms of hypersensitivity reactions during and following each administration of MARCFER.

MARCFER 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 observed for adverse effects for at least 30 minutes following each MARCFER injection (see section 4.4).

Administration: MARCFER must only be administered by the intravenous route. This may be by a slow intravenous injection or by an intravenous drip infusion.

MARCFER must not be used for intramuscular injection.

Adults and the elderly: The total cumulative dose of MARCFER, equivalent to the total iron deficit (mg), is determined by the haemoglobin level and body weight. The dose for MARCFER 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 MARCFER required in mg is determined from above calculation.

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

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

Dosage table stating the total amount of	**MARCFER in ml**	**:**

Body Weight	**Total amount of MARCFER 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 MARCFER has not been adequately studied in children and, therefore, MARCFER is not recommended for use in children.

Intravenous drip infusion: MARCFER must be diluted only in sterile 0.9% m/V sodium chloride solution:

• 2.5 ml MARCFER (50 mg iron)
in max. 50 ml sterile 0.9% m/V sodium chloride solution

• 5 ml MARCFER (100 mg iron)
in max. 100 ml sterile 0.9% m/V sodium chloride solution

• 10 ml MARCFER (200 mg iron)
in max. 200 ml sterile 0.9% m/V sodium chloride solution

For stability reasons, dilutions to lower MARCFER 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 MARCFER) in at least 15 minutes

• 200 mg iron (10 ml MARCFER) in at least 30 minutes

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

Injection into dialyser: MARCFER 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 MARCFER is contraindicated in cases of:

• hypersensitivity to the active substance, to MARCFER or any of its excipients listed in section 6.1
• known serious hypersensitivity to other parenteral iron products
• anaemias not attributable to iron deficiency
• iron overload or disturbances in utilisation of iron.

4.4 Special warnings and precautions for use

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.

The risk 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 reactions to parenteral iron complexes in patients with immune or inflammatory conditions (e.g. systemic lupus erythematosus, rheumatoid arthritis).

MARCFER 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 MARCFER 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 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 MARCFER 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, MARCFER 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 MARCFER.

4.6. Pregnancy and lactation

There are no adequate and well-controlled trials of MARCFER in pregnant women. A careful risk/benefit evaluation is therefore required before use during pregnancy and MARCFER should not be used during pregnancy unless clearly necessary (see section 4.4).

Iron deficiency anaemia occurring in the first trimester of pregnancy can in many cases be treated with oral iron. Treatment with MARCFER should be confined to second and third trimester if the benefit is judged to outweigh the potential risk for both the mother and the foetus.

Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development. Data on a limited number of exposed human pregnancies indicated no adverse effects of MARCFER on pregnancy or on the health of the foetus/newborn child.

Non metabolised MARCFER 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 MARCFER, 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 MARCFERin 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 I-SUCROZ, 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.

Reporting of sBPected adverse reactions

Reporting sBPected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any sBPected adverse reactions via:

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

5.2 Pharmacokinetic properties

Following intravenous injection of a single dose of MARCFER 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

Water for Injection

6.2 Incompatibilities

N.A.

6.3 Shelf life

2 Year

6.4 Special precautions for storage

Store in a dry place, protect from light, at the temperature not exceeding 30ºC.

6.5 Nature and Contents of Container

5ml solution for injection filled in amber glass ampoule. Such 5 ampoules place in tray and such one tray pack in carton together with instructions for medical use.

6.6 Special precautions for disposal and other handling

N.A.

7. Marketing authorisation holder

LOFORTE PHARMACEUTICALS LTD
4 Otunubi Street, Ori-Okuta,
Owutu, Ikorodu, Lagos
Nigeria

8. Marketing authorisation number(s)

N.A.

9. Date of first authorisation/renewal of the authorisation

N.A.

10. Date of revision of the text

N.A