Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

FERROSE 20MG/mL solution for injection.

2. Qualitative and quantitative composition

Each mL Contains:
Iron Sucrose Complex..... 20 mg
Eq. to Elemental Iron
Excipient with known effect:
Ferrose injection contains up to 7mg per mL of Sodium.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Liquid Injection that is dark brown, non-transparent, aqueous solution free from foreign particles filled in 5 mL amber colour glass ampoule.

4. Clinical particulars

4.1 Therapeutic indications

Ferrose 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,
- In active inflammatory bowel disease where oral iron preparations are ineffective,
- In chronic kidney disease where oral iron preparations are less effective than Ferrose.

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

4.2 Posology and method of administration

Monitor carefully patients for signs and symptoms of hypersensitivity reactions during and following each administration of Ferrose.
Ferrose 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 Ferrose administration (see section 4.4).
Posology
The cumulative dose of Ferrose must be calculated for each patient individually and must not be exceeded.
Calculation of dosage
The total cumulative dose of Ferrose, equivalent to the total iron deficit (mg), is determined by the haemoglobin level (Hb) and body weight (BW). The dose of Ferrose 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] = body weight [kg] x (target Hb - actual Hb) [g/l] x 0.24* + storage iron [mg]

Below 35 kg body weight: Target Hb = 13g/dL and storage iron = 15 mg/kg body weight

Above 35 kg body weight: Target Hb = 15g/dL and storage iron = 500 mg

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

The total amount of Ferrologic required is determined from either the above calculation or the following dosage table (based on a target haemoglobin of 130 g/l for a body weight of < 35 kg and 150 g/l for a body weight of > 35 kg).

Body weight [kg]	Total numbers of Ferrologic ampoules to be administered:			
	Hb 60 g/l	Hb 75 g/l	Hb 90 g/l	Hb 105 g/l
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

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

When the total necessary dose exceeds the maximum daily dose, the administration should be split.
When, after 1-2 weeks, the haematological parameters show no reaction, the initial diagnosis deserves reconsideration.

Calculation of the dosage for replacing blood losses and compensating autologous blood transfusions

If the amount of blood lost is known:
The administration of 200 mg of iron (= 2 ampoules of Ferrologic) causes an increase in haemoglobins that is equivalent to one blood unit (= 400 ml with 150 g/l of Hb).

Iron being replaced [mg] = total numbers of blood units lost x 200 or

Number of Ferrologic ampoules required = numbers of blood units lost x 2

If the haemoglobin value is reduced:
Use the afore-mentioned formula, considering that the iron deposits do not need to be restored.

Iron being replaced [mg] = body weight [kg] x 0.24 x (ideal Hb – real Hb) [g/l]

e.g.: body weight = 60 kg, Hb deficit = 10 g/l ⇒ amount of iron to be replaced = 150 mg = 1.5 ampoules (= 7.5 ml) of Ferrologic are required.

Posology

Adults and Elderly:

* 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.

Posology

Adults

5 - 10 mL of Ferrose (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 Ferrose has not been adequately studied in children and, therefore, Ferrose is not recommended for use in children

Method of administration

Ferrose 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

Ferrose 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:

Ferrose dose (mg of iron)	**Ferrose dose (mL of Ferrose)**	**Maximum dilution volume of sterile**	**Minimum Infusion Time**

		0.9% m/V NaCl Solution	
50mg	2.5mL	50mL	8 Minutes
100mg	5mL	100mL	15 Minutes
200mg	10mL	200mL	30 Minutes

For stability reasons, dilutions to lower Ferrose concentrations are not permissible.

Intravenous injection

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

Injection into venous line of dialysis machine

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

4.3 Contraindications

The use of Ferrose is contraindicated in the following conditions:

4.3.1 Hypersensitivity to the active substance, to Ferrose or any of its excipients listed in section 6.1

4.3.2 Known serious hypersensitivity to other parenteral iron products

4.3.3 Anaemia not caused by iron deficiency

4.3.4 Evidence of iron overload or hereditary 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 including iron sucrose. There have been reports of hypersensitivity reactions which progressed to Kounis syndrome (acute allergic coronary arteriospasm that can result in myocardial infarction, see section 4.8). In several studies performed in patients who had a history of a hypersensitivity reaction to iron dextran or ferric gluconate, Ferrose was shown to be well tolerated. For known serious hypersensitivity to other parenteral iron product see section 4.3.

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

Ferrose 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 Ferrose 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 should be used with caution in the case of acute or chronic infection. It is recommended that the administration of Ferrose 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 Ferrose at the injection site can lead to pain, inflammation and brown discoloration of the skin.

Ferrose 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.

4.5 Interaction with other medicinal products and other forms of interaction

As with all parenteral iron preparations, it is recommended that Ferrose is not administered concomitantly with oral iron preparations since the absorption of oral iron may be reduced.

4.6 Pregnancy and Lactation

Pregnancy

There is no data from the use of iron sucrose in pregnant women in the first trimester. Data (303 pregnancy outcomes) from the use of Ferrose in pregnant women in the second and third trimester showed no safety concerns for the mother or newborn. A careful risk/benefit evaluation is required before use during pregnancy and Ferrose 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 Ferrose 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. Foetal bradycardia may occur following administration of parenteral irons. It is usually transient and a consequence of a hypersensitivity reaction in the mother. The unborn baby should be carefully monitored during intravenous administration of parenteral irons to pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).

Breast-feeding

There is limited information on the excretion of iron in human milk following administration of intravenous iron sucrose. In one clinical study, 10 healthy breast-feeding mothers with iron deficiency received 100 mg iron in the form of iron sucrose. Four days after treatment, the iron content of the breast milk had not increased and there was no difference from the control group (n=5). It cannot be excluded that newborns/infants may be exposed to iron derived from Ferrose via the mother's milk, therefore the risk/benefit should be assessed. Preclinical data do not indicate direct or indirect harmful effects to the nursing child. In lactating rats treated with 59Fe-labelled iron sucrose, low secretion of iron into the milk and transfer of iron into the offspring was observed. Non metabolised iron sucrose is unlikely to pass into the mother's milk.

Fertility

No effects of iron sucrose treatment were observed on fertility and mating performance in rats.

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 Ferrose, patients should not drive or use machinery until the symptoms have ceased.

4.8 Undesirable effects

The most commonly reported adverse drug reaction in clinical trials with Ferrose was dysgeusia, which occurred with a rate of 4.5 events per 100 subjects. The most important serious adverse drug reactions associated with Ferrose are hypersensitivity reactions, which occurred with a rate of 0.25 events per 100 subjects in clinical trials. Anaphylactoid/anaphylactic reactions were reported only in the post-marketing setting (estimated as rare); fatalities have been reported. See section 4.4. The adverse drug reactions reported after the administration of Ferrose in 4,064 subjects in clinical trials as well as those reported from the postmarketing setting are presented in the table below.

System Organ Class	**Common (≥1/100,**	**Uncommon (≥1/1,000,**	**Rare (≥1/10 ,0 00,**	**Frequency not known1**
Immune system disorders		Hypersensitivity		Anaphylactoid/ ana phylactic reactions, angioedema
Nervous system disorders	Dysgeusia	Headache, Dizziness, Paraesthesia, Hypoaesthesia	Syncope, Somnole nce	Depressed level of consciousness, confusional state, loss of consciousness, anxiety, tremor
Cardiac disorders			Palpitatio ns	Bradycardia, tachycardia, Kounis

				syndrome
Vascular disorders	Hypotension, Hypertensio n	Flushing, Phlebitis		
Respiratory, thoracic and mediastinal disorders		Dyspnoea		
Renal and urinary disorders			Chromaturia	
Gastrointe stinal disorders	Nausea	Vomiting, Abdominal pain		
Skin and subcutaneous tissue disorders		Pruritus, rash		Urticaria, erythema
Musculosk eletal and connective tissue disorders		Muscle spasm, myalgia, arthralgia, pain in extremity, back Pain		
General disorders and administration site conditio	Injection/ infusion site reaction2	Chills, asthenia, fatigue, oedema peripheral, pain	Chest pain, hyperdro sis, pyrexia	Cold sweat, malaise, pallor, influenza like illness3

ns				
Investigati ons		Alanine aminotransferase increased, Aspartate	Blood lactate dehydrog enase	

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.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization 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 suspected adverse reactions via Pharmacy and Poisons Board- Pharmacovigilance Electronic Reporting System (PvERS); *https://pv.pharmacyboardkenya.org* .

4.9 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.

5. Pharmacological properties
5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Anti-anaemic preparation, iron, parenteral preparation, ATC code: B03AC
Mechanism of action
Iron sucrose, the active ingredient of Ferrose, 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 43 kDa. 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.
Clinical efficacy and safety
Chronic kidney disease
Study LU98001 was a single arm study to investigate the efficacy and safety of 100 mg iron as Ferrose for up to 10 sessions over 3–4 weeks in haemodialysis patients with iron deficiency anaemia (Hb >8 and <11.0g/dL, TSAT <20%, and serum ferritin ≤300µg/L who were receiving rHuEPO therapy. A Hb ≥11g/dL was attained in 60/77 patients. The mean increase in serum ferritn and TSAT was significant from baseline to the end of treatment (Day 24) as well as to the 2- and 5-weeks follow-up visit.
Study 1VEN03027 was a randomised study comparing Ferrose (1000 mg in divided doses over 14 days) and oral ferrous sulphate (325 mg 3 times daily for 56 days) in non-dialysis dependent chronic kidney disease patients (Hb ≤11.0 g/dL, serum ferritin ≤300 µg/L, and TSAT ≤25%) with or without rHuEPO. A clinical response (defined as Hb increase ≥1.0 g/dL and serum ferritin increase
≥160 µg/L) was more frequently observed in patients treated with Ferrose (31/79; 39.2%) compared to oral iron (1/82; 1.2%); p<0.0001'
Inflammatory Bowel Disease
A randomised, controlled study compared Ferrose (single IV dose of 200 mg iron once per week or every second week until the cumulative dose was reached) with oral iron (200 mg twice daily for 20 weeks) in patients with inflammatory bowel disease and anaemia (Hb<11.5g/dL). At the end of treatment, 66% of patients in the Ferrose group had an increase in Hb ≥2.0g/dL compared to 47% in the oral group (p=0.07).
Postpartum
A randomised, controlled trial in women with postpartum iron deficiency anaemia (Hb<9g/dL and serum ferritin <15µg/L at 24-48 hours post-delivery) compared 2 x 200mg iron given as Ferrose on Days 2 and 4 (n=22) and 200mg of oral iron given as ferrous sulphate twice daily for 6 weeks (n=21). The mean increase in Hb from baseline to Day 5 was 2.5g/dL in the Ferrose group and 0.7g/dL in the oral iron group (p<0.01).
Pregnancy
In a randomised, controlled study, women in their third trimester of pregnancy with iron deficiency anaemia (Hb 8 to 10.5 g/dL and serum ferritin <13µg/L) were randomized to Ferrose (individually calculated total dose of iron administered over 5 days) or oral iron polymaltose complex (100mg 3 x daily until delivery). The increase in Hb from baseline was significantly greater in the Ferrose group compared to the oral iron group at Day 28 and at delivery (p<0.01).

5.2 Pharmacokinetic properties

Distribution
The ferrokinetics of iron sucrose labelled with 52Fe and 59Fe were assessed in 6 patients with anaemia and chronic renal failure. In the first 6–8 hours, 52Fe was taken up by the liver, spleen and bone marrow. The radioactive uptake by the macrophage-rich spleen is considered to be

representative of the reticuloendothelial iron uptake. Following intravenous injection of a single 100 mg iron dose of iron sucrose in healthy volunteers, maximum total serum iron concentrations were attained 10 minutes after injection and had an average concentration of 538 µmol/L. 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 hours after injection of a Ferrose dose of 100 mg iron, corresponded to less than 5% of the dose. After 24 hours, the total serum iron concentration was reduced to the pre-dose level. Renal elimination of sucrose was about 75% of the administered dose.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of repeated dose toxicity, genotoxicity and toxicity to reproduction and development.

6. Pharmaceutical Particulars

6.1 List of Excipients

Sodium hydroxide
Water for injection
Potassium chloride

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6. 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.

6.3 Shelf-Life

Shelf life of the product as packaged for sale 3 years
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 (NaCl) solution
From a microbiological point of view, the product should be used immediately after dilution with sterile 0.9% m/V sodium chloride solution.

6.4 Special Precautions for storage

Do not store above 25℃.
Do not freeze.
Store in the original package/ Protect from light.

For storage conditions after dilution or first opening of the medicinal product, see section 6.3.

6.5 Nature and Content of container

5mL solution in amber colour ampoule (type I glass) packed in tray & carton along with package insert, in pack sizes of 5.

6.6 Special precautions for disposal and other handling

Ampoules should be visually inspected for sediment and damage before use. Use only those containing a sediment free and homogenous solution.

Ferrose must not be mixed with other medicinal products except sterile 0.9% sodium chloride solution for dilution.

For instructions on dilution of the product before administration, see section 4.2.

The diluted solution must appear as brown and clear.

Each ampoule or vial of Ferrose is intended for single use only.

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

7. Marketing Authorization Holder

GALAXY PHARMACEUTICAL LTD
Address: 1st FLOOR, DOCTOR'S PARK, 3RD PARKLANDS AVENUE
P.O. BOX 39107- 00623, NAIROBI
Country: KENYA
Telephone: 020-3748551/2/3/4

8. Marketing Authorization Number

H2009/19311/622

9. Date of first authorization/renewal of the authorization

22nd October, 2009

10. Date of revision of the text

24th February, 2026