IViron®
Iron Sucrose

FORMS AND PRESENTATION
IViron®: Solution for IV injection. 5x5 ml Ampoules.
COMPOSITION:
IViron®: Each 5ml ampoule contains: Elemental iron (as Iron Sucrose): 100mg. Excipients: sodium hydroxide, water for injection.
PHARMACOLOGICAL PROPERTIES
Pharmacodynamic Properties
Therapeutic class: Antianemic preparations.
ATC code: B03AC02.
A large number of non-covalently bound sucrose molecules are superficially surrounding the polynuclear iron (III)-hydroxide cores. This results in a complex whose molecular mass is approximately Mw 43 kD which is sufficiently large to prohibit renal elimination. Under physiological conditions, the resulting stable complex does not release ionic iron. In the polynuclear cores, the iron is bound in a similar structure as in the case of physiologically occurring ferritin. Following the administration of iron sucrose, physiological changes occur which involve the uptake of iron.
Preclinical safety data: there is a very low toxicity. In white mice, the LD_{50} for iron sucrose IV is superior to 200mg Fe/kg BW and consequently the therapeutic index is approximately 30 (200/7).
Pharmacokinetic Properties
The maximum iron levels (538µmol/l in average) are obtained 10 minutes after intravenous injection of a single dose of iron sucrose containing 100mg Fe(III) in healthy volunteers. The initial volume of distribution corresponds to the volume of serum which is approximately 3 liters. The iron injected is rapidly cleared from the serum with a terminal half life of approximately 6 hours. At steady state, the volume of distribution is about 8 liters, indicating a low iron distribution in the body water. A competitive exchange of iron to transferrin was observed due to the lower stability of iron sucrose in comparison to transferrin; which results in an iron transport of approximately 31mg Fe(III)/24 h. In the first 4 h after injection of iron, less than 5% of the total body clearance (approximately 20ml/min) is eliminated by the kidney. After 24 h, iron serum levels are reduced to the initial dose before injection. About 75% of the dosage of sucrose is excreted.
INDICATIONS
For the treatment of iron deficiency, IViron® is indicated in the following:
- where there is a clinical need to deliver iron rapidly to iron stores
- where oral iron preparations are ineffective in active inflammatory bowel disease
- in patients not tolerating oral iron therapy or are not complying.

CONTRAINDICATIONS
Iron sucrose is contra-indicated in cases of:
- known hypersensitivity to the drug
- overload or disturbances in utilisation of iron
- anaemia not attributed to iron deficiency
- pregnancy first trimester.

PRECAUTIONS
It is important to confirm the use of iron sucrose by appropriate laboratory tests (e.g. serum ferritin, or haematocrit, or haemoglobin (Hb), or erythrocyte count, or red cell indices – MCV, MCH, MCHC).
Allergic or anaphylactoid reactions may occur following parenteral administration of iron preparations: antihistamines should be used in mild allergic reaction, and adrenaline should be used immediately in serious anaphylactoid reaction. Risk of allergic or anaphylactoid reaction is particularly observed in bronchial asthmatic patients with a low iron binding capacity and/or folic acid deficiency. Caution is recommended in patients with serious hepatic dysfunction, an acute infection, a history of allergy or chronic infection.
If injection is administered too rapidly, hypotension may occur.
Paravenous leakage must be avoided. In case of accident leakage, proceed as follows: if the needle is still inserted, rinse with a small amount of 0.9% w/v NaCl solution. Instruct the patient to treat the point of injection topically with a mucopolysaccharid gel or ointment in order to accelerate iron elimination. Apply the gel or ointment gently. Avoid massage to prevent further spreading of the iron.
The course of interactions in children can be unfavorably influenced by parenteral administration of iron preparations.
It is unlikely that iron sucrose has an influence on the ability to drive and use machines.
PREGNANCY AND LACTATION
Iron sucrose is not teratogenic or embryocidal in non-anaemic pregnant animals according to reproductive toxicity studies. However, during the first trimester, the use of parenteral iron preparations should be discouraged; caution is recommended during the second and third term. Non metabolised iron sucrose is unlikely excreted into breast milk.
DRUG INTERACTIONS
As with all parenteral iron preparations, iron sucrose should not be administered concomitantly with oral iron preparations since the absorption of oral iron is decreased. Therefore, treatment with oral iron should be started at least 5 days after the last injection of iron sucrose.
Incompatibilities: iron sucrose must only be mixed with 0.9% w/v NaCl solution. No other therapeutic agents should be used.
ADVERSE EFFECTS
Anaphylactic like reactions may occur very rarely.
Occasionally, metallic taste, nausea, vomiting, headache and hypotension have been reported with a frequency of ≥1%.
Less frequently, abdominal disorders, muscular pain, fever, paraesthesia, urticaria, flushing, oedema of the extremities and anaphylactoid (pseudoallergic) reactions have occurred. At the site of injection, phlebitis and venous spasm have been observed.
DOSAGE AND ADMINISTRATION
Administration of IViron® has to be exclusively intravenously by drip infusion, by slow injection or directly into the venous limb of the dialyser. IViron® is not suitable for IM use and for total dose infusion (TDI), where the full dose of iron required, representing the patient's total iron deficit is administered in one complete infusion.
A test dose of IViron® in a new patient should be given by the chosen method of administration as follows: 1 to 2.5ml IViron® (20 to 50mg iron) in adults, 1ml (20mg iron) in children > 14 kg BW and half the daily dose (1.5mg/kg) in children < 14 kg BW. Cardiopulmonary resuscitation facilities must be available. After a waiting period of at least 15 min following administration, without any adverse reactions, the remaining portion of the initial dose can be given.
Infusion: administration of IViron® by drip infusion is preferred in order to reduce the risk of hypotension and paravenous injection. Dilute 1ml IViron® (20mg iron) exclusively in max. 20ml of 0.9% w/v NaCl solution, immediately before infusion (i.e. 5ml in max. 100ml 0.9% w/v NaCl up to 25ml in max. 500ml 0.9% w/v NaCl). Infusion of the solution should be at the following rate: 100ml in at least 15 min; 200ml in at least 30 min; 300ml in at least 1.5 h; 400ml in at least 2.5 h; 500ml in at least 3.5 h.
IViron® may be diluted in less than the specified amount of 0.9% w/v NaCl solution, in some clinical circumstances, producing a higher IViron® concentration. However, the rate of infusion must be precised according to the amount of iron given per minute (e.g. 2 ampoules IViron® = 200mg iron should be infused in at least 30 min; 5 ampoules IViron® = 500mg iron should be infused in at least 3.5 h). Due to stability reasons, dilutions to lower IViron® concentrations are not allowed.
Intravenous injection: IViron® may be administered by slow intravenous injection at a rate of 1ml undiluted solution per minute (i.e. 5 min / ampoule) not exceeding 2 ampoules of IViron® (200mg iron) per injection. Extend the arm of the patient following an injection.
Injection into dialyser: under the same procedures as those outlined for IV injection, IViron® may be administered directly into the venous limb of the dialyser.
Calculation of dosage: the dose of IViron® must be determined for each individual patient according to the total iron deficit calculated with the following formula:

Total iron deficit [mg] = BW [KG] x (target Hb - actual Hb) [g/l] x 0.24* + depot iron [mg]

• Below 35 kg BW: target Hb = 130 g/l and depot iron = 15mg/kg BW

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

* Factor 0.24 = 0.0034 x 0.07 x 1000 (Iron content of Hb 0.34%; Blood volume 7% of BW; Factor 1000 = conversion from g to mg).

Total amount of IViron® to be administered [in mg] = $\frac{\text{Total iron deficit [mg]}}{\text{20 mg/ml}}$

Total amount of IViron® (in ml) required is determined as per the following dosage table:

BW	Hb 60g/l	Hb 75g/l	Hb 90g/l	Hb 105g/l
5 kg	8	7	6	5
10 kg	16	14	12	11
15 kg	24	21	19	16
20 kg	32	28	25	21
25 kg	40	35	31	26
30 kg	48	42	37	32
35 kg	63	57	50	44
40 kg	68	61	54	47
45 kg	74	66	57	49
50 kg	79	70	61	52
55 kg	84	75	65	55
60 kg	90	79	68	57
65 kg	95	84	72	60
70 kg	101	88	75	63
75 kg	106	93	79	66
80 kg	111	97	83	68
85 kg	117	102	86	71
90 kg	122	106	90	74

Split the total necessary dose if it exceeds the maximum allowed single dose. After 1-2 weeks, the original diagnosis should be reconsidered if no response of the haematological parameters is observed.

Calculation of dosage for iron replacement secondary to blood loss and to support autologous blood donation:

• *If the quantity of blood lost is known:* the administration of 2 ampoules of IViron® (200mg iron) results in an increase in Hb concentration (150 g/l) which is equivalent to one unit blood (400ml), so the method of calculation will be as follows:

- the total iron quantity to be replaced [mg] = number of blood units lost x 200;
- amount of IViron® needed [mg] = number of blood units lost x 10.

• *If Hb concentration is known:* the previous formula is used considering that the depot iron does not need to be restored. Therefore, the total iron quantity to be replaced [mg] = BW [kg] x 0.24 x (target Hb – actual Hb) [g/l].

e.g.: BW 60 kg, Hb deficit = 10 g/l; iron to be replaced ≈ 150mg i.e 7.5ml IViron® are needed.

Posology:

- *Adults and the elderly:* 5 – 10ml IViron® (100 – 200mg iron) twice or 3 times a week depending on the Hb level.

The maximum tolerated single dose:

As injection: 10 ml IViron® (200mg iron) injected in at least 10 min.

As infusion: in case of clinical need, the single dose may be increased to 0.35ml IViron®/kg BW (7mg iron/kg BW); do not exceed 25ml IViron® (500mg iron), diluted in 500ml 0.9% w/v NaCl infused over at least 3.5 h, once a week.

- *Children:* 0.15ml IViron®/kg BW (3mg iron/kg BW) twice or 3 times a week depending on the Hb level.

The maximum tolerated single dose:

0.35ml IViron®/kg BW (7mg iron/kg BW) diluted in 0.9% w/v NaCl and infused over at least 3.5 h, once a week.

Instructions for use and handling: Visually inspected ampoules for sediment and damage should be performed before use. Sediment free and homogenous solution must be only used.

Once opened, IViron® should be administered immediately. IViron® diluted with 0.9% w/v NaCl solution should be used within 12 h if stored below 25°C in the day light.

OVERDOSAGE

Overdosage may lead to acute iron overloading responsible of haemosiderosis. In case of overdosage, patients should be treated with supportive measures and, if required an iron chelating agent.

STORAGE CONDITIONS

Store below 30°C, protected from light. Do not freeze.

Keep in original pack in intact conditions.

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This is a medicament

- A medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you
- Follow strictly the doctor's prescription, the method of use, and the instructions of the pharmacist who sold the medicament
- The doctor and the pharmacist are experts in medicine, its benefits and risks
- Do not by yourself interrupt the period of treatment prescribed for you
- Do not repeat the same prescription without consulting your doctor
- Medicament: keep out of reach of children

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