MEDLEY PHARMACEUTICALS

M-JECT INJ

Iron Sucrose Injection 20mg/ml

Formulation

Each ml contains 20 mg Iron Sucrose as elemental iron (100 mg/ 5 ml)

Description

Iron sucrose injection is a dark- brown colloidal solution for intravenous use. It has a-molecular weight of approximately 34,000 - 60,000 Daltons and a proposed structural formula:

$[Na_2Fe_5O_8.3\ (H2O)_n.\ m\ (C_{12}H_{22}O_{11})$ Where: n is the degree of iron polymerization and m is the number of sucrose molecules associated with the iron (III)-hydroxide. Each ml contains 20 mg elemental iron as iron sucrose in water for injection. It is available in 5 ml ampoule.

Pharmacology & Toxicology

The polynuclear iron (III)-hydroxide cores are superficially surrounded by a large number of non-covalently bound sucrose molecules resulting in a complex whose molecular mass is approximately Mw 43 KD. This is sufficiently large to prohibit renal elimination. The resulting complex is stable and does not release ionic .iron under physiological conditions. The iron in the polynuclear cores is bound in a similar structure as in the case of physiologically occurring ferritin.

Administration of iron sucrose causes physiological changes which involve the uptake of iron.

Iron sucrose possesses a low toxicity with LD_{50}, of greater than 200mg Fe/kg body weight when administered to mice. It has a therapeutic index about 30(200/7).

Package Form:

5 ml ampoule (Box of 5's)

Caution:

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Avoid freezing. Injection should not be used If container Is leaking, Solution is cloudy or It contains undissolved particles. Improper storage conditions may deteriorate medicine quality.

Store in cool and dry place below 25°C. Keep all medicines out of children reach.

See package insert for full prescribing Information

Storage:

Store at temperatures not exceeding 30°C.

Pharmacokinetics:

The pharmacokinetics of Iron (Ill)-hydroxide sucrose complex was investigated after intravenous injection of a single dose containing 100 mg Fe (III) in healthy volunteers. The maximum iron level averaging 538 micromole/L, are obtained 10 minutes after injection. The volume of distribution of the central compartment corresponds in good agreement to the volume of serum (approx 3L).

The iron injected is quickly cleared from the serum, the terminal half-life Is approx.6h. The volume of distribution at steady state is about 8L, which indicates a low iron distribution in the body water. Due to the lower stability of Iron (III)-hydroxide sucrose complex in comparison to transferrin a competitive exchange of iron to transferrin was observed. This results In an iron transport of approx. 31 mg Fe(III)/24h.

Renal elimination of iron, occurring in the first 4 h after injection, corresponds to less than 5% of the total body clearance (approx. 20ml/min). After 24 h the serum levels of iron are reduced to the predose iron levels and about 75% of the dosage of sucrose is excreted.

Indications

Iron sucrose is indicated in the treatment of Iron deficiency anemia in patients undergoing chronic hemodialysis who are receiving supplemental erythropoietin therapy.

Dosage & Administration

Administration

Iron sucrose is used as a source of iron for iron-deficiency anemia. Iron sucrose is to be administered intravenously by slow injection or by infusion, or when used in haemodialysis patients, into the venous limb of the dialyses.

Infusion: Iron sucrose injection may preferably be administered by infusion. Iron sucrose may be given undiluted at the rate of 20 mg/minute, after a test dose of 20 mg of iron has been given over 1 to 2 minutes.

Alternatively, 100 mg is diluted in a maximum of 100 ml of 0.9% NaCI and the first 25 mg given as a test dose over 15 minutes; the remaining portion is given at a rate not exceeding 50 ml per 15 minutes.

Slow Intravenous Injection: Iron sucrose injection may be administered by slow intravenous injection at a rate of 1 ml undiluted per minute (i.e. 5 minutes per 5 ml ampoule) not exceeding 5 ml iron sucrose injection (100 mg iron) per injection. After an injection, extend the arm of the patient.

Injection Into dialyzer: Iron sucrose injection may be administered directly into the venous limb of the dialyzer under the same conditions as for Intravenous injection.

Dosage

Calculation of dosage: The dosage has to be Individually adapted 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) x0.24*-(4-depot iron (mg) Up to 35 kg body weight target Hb = 130 g/L resp. depot iron =,15 mg/kg body weight. Above 35 kg body weight target Hb = 150 g/L resp. depot Iron = 500mg

Factor 0.24 = 0 0034 x 0.07 x 1000

(Iron content of hemoglobin 0.34% blood volume = 7% of body weight/Factor 1000=conversion from g to mg) Total amount of iron sucrose injection to be administered (in ml) = Total iron deficit (mg)/200mg/ml

If the total necessary dose exceeds the maximum allowed single dose, then the administration has to be split. If no response of the hematologlcal parameters Is observed after 1 to 2 weeks the original diagnosis should be reconsidered.

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

The required iron sucrose injection dose to compensate the iron deficit is calculated according the following formulas:

Number of Ampoules Needed				
Body Weight (kg)	Hb 60 g/L	Hb 75 g/L	Hb 90 g/L	Hb 105 g/L
5	1.5	1.5	1.5	1.0
10	3.0	3.0	2.5	2.0
15	5.0	4.5	3.5	30
20	6.5	5.5	5.0	4.0
25	8.0	7.0	6.0	5.5
30	9.5	8.5	7.5	6.5
35	12.5	11.5	10.0	90
40	13.5	12.0	11.0	9.5
45	15.0	13.0	11.5	10.0
50	16.0	14.0	12.0	10.5
55	17.0	15.0	13.0	11.0
60	18.0	16.0	13.5	11/5
65	19.0	16.5	14.5	12.0
70	20.0	17.5	15.0	12.5
75	21.0	18.5	16.0	13.0
80	22.5	19.5	16.5	13.5
85	23.5	20.5	17.0	14.0
90	24.5	21.5	18.0	14.5

If the quantity of blood lost Is known: the administration of 200 mg l.V. Iron (= 10ml iron sucrose injection) results in an increase in hemoglobin which is equivalent to 1 unit Wood (-400ml with 150 g/L Hb content). Iron to be replaced (mg) * number of blood units lost x 200 or amount of Iron sucrose injection needed (ml) = number of blood units lost x 10. If the Hb level Is reduced: use

the previous .formula considering that the depot Iron does not need to be restored. Iron to be replaced (mg) = body weight x 0.24 x (target Hb-actual Hb) (g/L). e.g. body weight 60 kg, Hb deficit = 10g/L => Iron to be replaced 150 mg => 7.5ml Iron sucrose injection needed

Normal Physiology

Adult and the Elderly:

5-10 ml iron sucrose injection (100 to 200 mg iron) two to three times a week depending on the hemoglobin level. Frequency of dosing should be not more than three times weekly

Children:

0.15 ml iron sucrose injection/kg body weight (= 3 mg iron/kg bw) twice or three times a week depending on the hemoglobin level.

Maximum tolerated single dose

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Adults and the Elderly:

As injection; 10ml iron sucrose injection (200 mg iron) injected In at least 10 minutes

As infusion: If the clinical situation demands the single dose may be increased to 0.35 ml iron sucrose injection/kg body weight (= 7 mg iron/kg bw) not exceeding 25 ml iron sucrose injection (500 mg iron). diluted to 500ml 0.9% NaCI infused over at least 3.5 hours once a week.

Adverse Reactions

Very rarely allergic anaphylactic like reactions may occur.

Occasionally the following undesirable effects have been reported with a frequency of not less than 1%: metallic taste, headache, nausea, vomiting, diarrhea, hypotension, elevated liver enzymes cramps/ leg cramps, chest pain, dizziness, dyspnea, pneumonia, cough, pruritus. Less frequently paresthesia, abdominal disorders, muscular pain, fever, urticaria, flushing, edema of the extremities, dyspnea and anaphylactoid (pseudoallergic) reactions have been reported In the region of the punctured vein, phlebitis and venous spasm have been observed.

Contraindications

The use of iron sucrose is contradicted in cases of:

Anemia not caused by iron deficiency

Iron overload or disturbances in utilization of Iron

Known hypersensitivity to iron mono- or disaccharide complexes

Precautions

Iron sucrose should be used with caution in patients with a history of asthma, eczema, anaphylaxis or other allergic disorder.

Pregnancy & Lactations

Animal teratology studies have shown that iron sucrose has no teratogenic effect and does not cause abortion in non-anemic animals. But use of parenteral iron preparations during} the first

three month-. has to be discouraged. During the second and third term, the application has to be done with caution. None of its metabolites can be excreted into the breast milk.

Drug Interactions

As with all parenteral administered iron preparations iron sucrose should not be administered concomitantly with oral iron preparations since the absorption of oral iron can be reduced. Therefore an oral iron therapy should at least be started 5 days after the last injection.

Over dosage

Dosages of iron sucrose in excess of iron needs may lead: to accumulation of iron in storage sites leading to hemosiderosis. Over dosage should be treated with efficient procedure. Iron binding preparations should be used when necessary.