

New Zealand Data Sheet

Ferrosig Injection

Iron polymaltose 50 mg/mL

Presentation

A slightly viscous, dark reddish brown liquid. Odour faintly malt-like. Each 2 mL ampoule of FERROSIG contains the equivalent of 100mg of iron.

Uses

Actions

FERROSIG is an aqueous, approximately isotonic solution for intramuscular injection. The complex is stable over a wide pH range (1-14) and each 2 mL ampoule contains the equivalent of 100 mg iron. Pharmacological tests have shown that the complex has a low toxicity with a LD₅₀ (intravenous) of 400mg iron per kg in white mice.

Pharmacokinetics

A study was conducted on 12 anaemic women aged from 20-45 years. After an intravenous infusion of 100 mg elemental iron, comprising 2 mL of Iron Polymaltose Injection diluted in 48 mL 0.9% sodium chloride, at a rate of 1.7 mL/min. (ie 50 mL per 30 minutes) a mean C_{max} (in serum) of 25.1 µg/mL iron was observed. The mean T_{max} was 0.75 hours and the mean terminal half-life 22.4 hours. The mean residence time (MRT) was 20.2 hours.

When injected intramuscularly the iron polymaltose evokes a local inflammatory response and is transported via the lymphatics to the regional lymph nodes without being broken down (reactive absorption). It then enters the blood, reaching its maximum concentration in about 24 hours. The circulating iron polymaltose is taken up by the cells of the reticulo-endothelial system, which slowly ionise it to Fe³⁺ and polymaltose. The majority of Fe³⁺ is bound to transferrin and transported to the bone marrow where it is incorporated into haemoglobin, the remainder is contained within the storage forms, haemosiderin and ferritin, or incorporated into myoglobin or haem-containing enzymes. Only very small amounts of iron are excreted. The conservation of body iron and the lack of an excretory mechanism for excess iron may lead to iron overload if iron intake is excessive. Polymaltose is either metabolised or excreted.

Indications

For the prevention and treatment of iron deficiency anaemia in the following circumstances:

- When oral therapy is contraindicated
- When enteric absorption of iron is defective
- When patient non-compliance or persistent gastrointestinal intolerance makes oral therapy impractical
- Treating iron deficiency anaemia of prematurity and that occurring in geriatric patients
- Treating iron deficiency states discovered in the third trimester of pregnancy
- Anaemia resulting from excessive blood loss
- Where contact between the doctor and patient occurs at irregular intervals

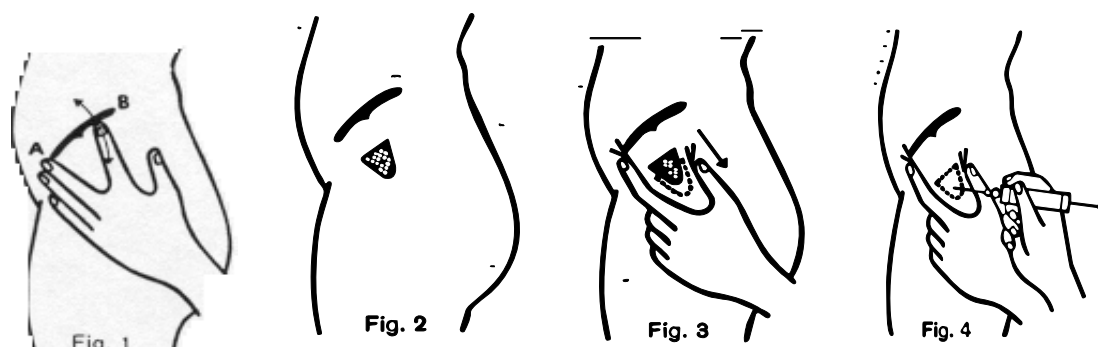
Dosage and Administration

Intramuscular Use

Technique of Injection

The technique of injection is of crucial importance. Iron Polymaltose should never be injected into the arm or other exposed areas. The wrong method may result in pain and discolouration of the skin.

The following method of ventro-gluteal injection according to HOCHSTETTER is recommended instead of the normal method of injection in the top outer quadrant of the gluteus maximus muscle:



- The length of the needle should be at least 5-6cm. The lumen of the needle should not be too wide.
- The site of injection is determined as follows (See Fig 1): First point A is found, corresponding to the ventral iliac spine. If the patient lies on the right side, for instance, the middle finger of the left hand is placed on point A. The index finger is extended away from the middle finger, so that it comes to lie below the iliac crest, at point B. The triangle lying between the proximal phalanges of the middle and index fingers

represents the site of injection. This is disinfected in the usual way (Fig 2).

- Before the needle is inserted, the skin over the site of injection is pulled down, about 2cm (Fig 3), to give an S-shaped puncture channel. This prevents the injected solution from running back into the subcutaneous tissues and discolouring the skin.
- The needle is introduced more or less vertically to the skin surface, angled to point towards the iliac crest rather than the hip joint (Fig 4).
- After the injection, the needle is slowly withdrawn and pressure from a finger applied beside the puncture site. This pressure is maintained for about one minute.
- The patient should move about after the injection.

Intravenous Use

Total dose infusion of iron polymaltose complex is recommended only when the intramuscular route is impractical or unacceptable and when bone marrow shows no stored iron. It is suitable for use in hospitals only.

The total dose to be administered, calculated from the dosage table, is aseptically added to 500 mL of sterile, normal saline (up to 2500mg may be given in 500 mL).

Notes

- Do not inject the iron into the tube of the administration set.
- The first 50 mL should be infused slowly (5-10 drops/minute) and the patient observed carefully. If this is well tolerated, the rate may be increased to 30 drops/minute (based on a drop volume of 0.067mL).
- To avoid nausea and epigastric troubles the infusion rate should not be excessive.
- The infusion should not be mixed with any other therapeutic agents. If mixed with acidic substances or other substances with a strong reducing effect toxic iron compounds may be liberated from the compound.

Calculation of Required Dose

The figures in the accompanying dosage table have been calculated using the following formula taken from GANZONI (Schweiz. Med. Wschr. 100, 301-619, 1970):

$$\text{Iron dose (mg)} = \text{body weight (kg)} \times \underbrace{(\text{target Hb} - \text{actual Hb in g/L}) \times 0.24^*}_{\text{Hb-iron deficiency}} + \text{iron depot}$$

* The factor 0.24 = 0.0034 x 0.07 x 1000

(for the purposes of this calculation iron content of the haemoglobin = 0.34%, blood volume = 7% of the body weight, 1000 is the conversion from grams to milligrams).

The above formula can also be used to calculate the total iron deficit.

Up to 34 kg body weight: target Hb = 130 g/L, iron depot = 15 mg/kg body weight

(for a patient weighing 34 kg the iron depot is 34 x 15 = 500 mg)

Over 34 kg body weight: target Hb = 150 g/L, iron depot = 500 mg

Example of Calculation

Assuming a patient weighing 60 kg, target Hb 150 g/L, actual Hb 60 g/L and the need for an iron depot of 500 mg then:

Hb-iron deficiency = 60 x (150-60) x 0.24 = 1296 mg + 500 mg = 1800 mg iron

Therefore the patient requires 1800 mg iron or 18 ampoules.

Dosage Table

Dosage table for the determination of the total millilitres of FERROSIG injection required.

Body weight kg	Hb 60g/L		Hb 75g/L		Hb 90g/L		Hb 105g/L	
	mL	ampoules	mL	ampoules	mL	ampoules	mL	ampoules
5	3	1.5	3	1.5	3	1.5	2	1
10	6	3	6	3	5	2.5	4	2
15	10	5	9	4.5	7	3.5	6	3
20	13	6.5	11	5.5	10	5	8	4
25	16	8	14	7	12	6	11	5.5
30	19	9.5	17	8.5	15	7.5	13	6.5
35	25	12.5	23	11.5	20	10	18	9
40	27	13.5	24	12	22	11	19	9.5
45	30	15	26	13	23	11.5	20	10
50	32	16	28	14	24	12	21	10.5
55	34	17	30	15	26	13	22	11
60	36	18	32	16	27	13.5	23	11.5
65	38	19	33	16.5	29	14.5	24	12
70	40	20	35	17.5	30	15	25	12.5

Body weight kg	Hb 60g/L		Hb 75g/L		Hb 90g/L		Hb 105g/L	
	mL	ampoules	mL	ampoules	mL	ampoules	mL	ampoules
75	42	21	37	18.5	32	16	26	13
80	45	22.5	39	19.5	33	16.5	27	13.5
85	47	23.5	41	20.5	34	17	28	14
90	49	24.5	43	21.5	36	18	29	14.5

Administer 2 mL by intramuscular injection every second day until the total dose is attained or administer 4 mL at longer intervals. Regular determination of Hb level is recommended.

Maximum Single Daily Dose by Intramuscular Injection

Infants up to 5 kg body weight: 0.5 mL

Children of 5-10 kg body weight: 1 mL

Patients weighing >10 kg to 45 kg: 2 mL

Adults: 4 mL

Contraindications

FERROSIG should not be given to patients presenting with any of the following conditions:

- Hypersensitivity to iron(III) hydroxide polymaltose complex
- Anaemia not caused by simple iron deficiency (e.g. haemolytic anaemia, megablastic anaemia caused by Vitamin B₁₂ deficiency, disturbances in erythropoiesis, hypoplasia of the marrow)
- Iron overload (e.g. haemochromatosis, haemosiderosis)
- Chronic polyarthritis
- Bronchial asthma
- Infectious renal complaints in acute phase
- Uncontrolled hyperparathyroidism
- Decompensated hepatic cirrhosis
- Infectious hepatitis
- During the first trimester of pregnancy

As elemental iron tends to accumulate in inflamed tissues parenteral iron should not be given to patients with severe inflammation or infection of the kidney or liver.

Warnings and Precautions

Since parenteral use of complexes of iron and carbohydrates has resulted in fatal anaphylatoid reactions, iron polymaltose should be used only in patients

in whom a clearly established indication for parenteral iron therapy exists, confirmed by appropriate laboratory tests.

Anaphylactoid reactions occur most frequently within the first several minutes of administration and are generally characterised by sudden onset of respiratory difficulties, tachycardia and hypotension. An initial test dose of 25 mg of iron polymaltose should be given prior to the first therapeutic dose of the drug. Adrenaline and facilities for cardio-pulmonary resuscitation must be available. In the case of a mild allergic reaction, administer antihistamines.

Patients with bronchial asthma, low iron binding capacity or folic acid deficiency are particularly at a risk of an allergic or anaphylactoid reaction. Caution is also recommended in patients with a history of allergic disorders, hepatic insufficiency or cardiovascular disease.

Patients with rheumatoid arthritis and possibly other inflammatory diseases (eg ankylosing spondylitis, lupus erythematosus) may be at particular risk of delayed reactions, including fever and exacerbation or reactivation of joint pain.

Iron may increase the pathogenicity of certain micro-organisms. The use of intramuscular iron in neonates has been associated with an increased incidence of Gram negative sepsis, principally infections caused by *E. coli*.

Unwarranted administration of parenteral iron preparations may cause excess storage of iron and a syndrome similar to haemosiderosis in patients whose anaemia is not attributable to iron deficiency eg. those with haemoglobinopathies.

Use in pregnancy and lactation

FERROSIG should not be administered in the first trimester of pregnancy. FERROSIG should only be administered in the second and third trimester of pregnancy if the benefits of treatment outweigh the potential risk to the foetus. No controlled studies are available on animals or on pregnant women.

Adverse Effects

Adverse reactions to parenteral FERROSIG have only been reported infrequently. However, the following reactions are known to have occurred after parenteral iron therapy:

General

- Flushing, sweating, chills and fever
- Chest and back pain

Following intramuscular injection

- Pain at injection site
- Local inflammation with inguinal lymphadenopathy
- Lower quadrant abdominal pain

Hypersensitivity

- Anaphylaxis

Gastrointestinal

- Nausea and vomiting

Central Nervous System

- Headache
- Dizziness

Musculoskeletal

- Joint and muscle pain
- Arthralgia
- Sensation of stiffening of the arms, legs or face

Cardiovascular

- Faintness
- Syncope
- Tachycardia
- Hypotension
- Circulatory collapse

Respiratory

- Bronchospasm with dyspnoea

Haematological

- Generalised lymphadenopathy

Dermatological

- Rash
- Urticaria
- Angioneurotic oedema

Adverse reactions may be delayed by 1-2 days after treatment with FERROSIG Injection.

Interactions

As with all parenteral iron preparations, FERROSIG ampoules should not be administered concomitantly with oral iron preparations as the absorption of oral iron is reduced. Oral iron therapy should not commence until at least one week after the last iron injection.

Concomitant administration of angiotensin converting enzyme (ACE) inhibitors may increase the incidence of adverse effects associated with parenteral iron preparations eg erythema, abdominal cramps, nausea, vomiting and hypotension.

Overdosage

Overdosage of iron causes haemosiderosis and consequent cirrhosis of the liver, diabetes and heart failure. Periodic monitoring of serum ferritin may be useful in recognising a deleterious, progressive accumulation of iron.

Pharmaceutical Precautions

The ampoules should be stored below 25°C. Do not freeze. Protect from light.

Shelf Life; 36 months from date of manufacture stored at or below 25°C

When diluted in saline the solution should be used within 12 hours.

Medicine Classification

Prescription Medicine.

Package Quantities

Cartons of 5 x 2 mL ampoules, each ampoule containing 318 mg iron polymaltose equivalent to 100 mg iron III (50 mg per mL).

Further Information

FERROSIG contains a macromolecular spherocolloidal complex of iron(III) hydroxide and the carbohydrate ligand polymaltose. The complex has a molecular weight of about 462,000.

The aqueous colloidal solution is sterile, pyrogen-free and approximates the pH and tonicity of the tissues.

Excipients

Water for injection, sodium hydroxide (for pH adjustment).

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