SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

HAEMOJET Ampoules in Solution for I.M. Injection.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Ampoule (2 ml) contains Elemental Iron 100 mg (As Ferric Hydroxide Polymaltose).

For a full list of excipients see Section 6.1.

3. PHARMACEUTICAL FORM

Solution for I.M. Injection.

Very dark reddish brown solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For the prevention and treatment of iron deficiency anemia 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 anemia of prematurity and that occurring in geriatric patients.
- Treating iron deficiency anemia states discovered in third trimester of pregnancy.
- Anemia resulting from excessive blood loss.
- Where contact between the doctor and patients occurs at irregular intervals.

4.2 Posology and method of administration

Technique of Injection:

The technique of injection is of crucial importance. HAEMOJET Ampoules should never be injected into the arm or other exposed areas. The wrong method may result in pain and discoloration 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 5-6 cm. The lumen of the needle should not be too wide.
- According to HOCHSTETTER, 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 2 cm (Fig. 3), to give an S-shaped puncture channel. This prevents the injected solution from running back into the subcutaneous tissues and discoloring 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. The pressure is maintained for about one minute.
- The patient should move about after the injection.

Dosage Table (for the determination of the total milliters of HAEMOJET Ampoules required):

Body weight	**Hb 60 g/l**		**Hb 75 g/l**		**Hb 90 g/l**		**Hb 105 g/l**	
kg	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
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 IM injection every second day until the total dose is attained or administer 4 ml at longer intervals. Regular determination or Hb level is recommended.

Maximum single daily dose by intramuscular injection:

Infants up to 5 kg body weight: 0.5 ml.

Children up to 5 – 10 kg body weight: 1 ml.

Patients weighing > 10 kg to 45 kg: 2 ml.

Adults: 4 ml.

4.3 Contraindications

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

- Hypersensitivity to iron (III) hydroxide polymaltose complex.

- Anemia not caused by simple iron deficiency (e.g. hemolytic anemia, megaloblastic anemia caused by vitamin B_{12} deficiency, disturbances in erythropoiesis, hypoplasia of the marrow).
- Iron over load (e.g. haemochromatosis, haemosiderosis).
- Ostler-Rendu-Weber syndrome.
- Chronic polyarthritis.
- Bronchial asthma.
- Infectious renal complaints in acute phase.
- Uncontrolled hyperparathyroidism.
- Decompensated hepatic cirrhosis.
- Infectious hepatitis.

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.

4.3 Special warnings and precautions for use

Parentally administered iron preparation can cause allergic or anaphylactic reactions. In the case of a mild allergic reaction. Antihistamines should be administered immediately. Facilities for cardiopulmonary resuscitation must be available. Caution is recommended in patients with allergies and hepatic and renal insufficiency. The incidence of undesirable side effects in patients with angiocardiopathy may increase the related cardiovascular complications.

Patients with bronchial asthma, with low iron binding capacity and/or folic acid deficiency are particularly at risk of an allergic or anaphylactic reaction.

Parenterally administered iron preparations can unfavorably influence the course of infections in children.

Some cases of anaphylactic reactions after parenteral administration of iron having been described, it is recommended to initiate the treatment with a test dose to test the sensitivity of the patient.

4.5 Interaction with other medicinal products and other forms of interaction

As with all parenteral iron preparations, HAEMOJET 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, e.g. erythema, abdominal cramps, nausea, vomiting and hypotension.

4.6 Pregnancy and lactation

HAEMOJET Ampoules should not be administered in the first trimester of pregnancy. HAEMOJET Ampoules should only be administered in the second and third trimester of pregnancy if the benefits of treatment outweigh the potential risk to the fetus.

No control studies are available on animals or on pregnant women.

4.7 Effects on ability to drive and use machines

None Known.

4.8 Undesirable effects

The following reactions are known to have occurred after parenteral iron therapy:

Local reactions may include pain at the site of injection, local inflammation with inguinal lymphadenopathy, and lower quadrant abdominal pain.

Systemic reactions after this form of administration are rare but may include anaphylaxis.

Delayed systemic reactions: may include dizziness, syncope, a sensation of stiffening of the arms, legs or face, chest and pack pain, arthralgia, chills, fever, rash, urticarial, angioneurotic oedema and generalized lymphadenopathy.

4.9 Overdose

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

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Hematinic.

ATC code: B03A B05.

Iron, an essential mineral is a component of hemoglobin, myoglobin and a number of enzymes (e.g. cytochromes, catalase, peroxidase).

The total body content of iron is approximately 50 mg/kg in men (3.5 g in the average 70 kg man), and 37 mg/kg in women. Iron is primarily stored as hemosiderin or aggregated ferritin, found in the reticuloendothelial system and hepatocytes. Approximately two thirds of total body iron are in circulating red blood cell mass in hemoglobin, the major factor in oxygen transport.

Iron deficiency can affect muscle metabolism, heat production and catecholamine metabolism and has been associated with behavioral or learning problems in children.

5.2 Pharmacokinetic properties

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 reticuloendothelial system, which slowly ionize it to Fe^{3+} and polymaltose. The majority of Fe^{3+} is bound to transferrin and transported to the bone marrow where it is incorporated into hemoglobin, the remainder is contained within the storage forms, hemosiderin and ferritin, or incorporated into myoglobin or hem-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 metabolized or excreted.

5.3 Preclinical safety data

Single dose toxicity (Acute):

Acute toxicity of Iron Hydroxide Polymaltose is very low, it is about 10 times smaller than that of ferrous sulphate.

When administered orally to mice or rats with LD50 values of drug Ion Polymaltose complex is more than 2.000 mg / kg body weight. Due to the necessity of a large volume of test solution, and the fact that the Iron Polymaltose is practically non-toxic, further testing of higher doses of the drug has not been.

Repeat-dose toxicity (Chronic):

Study of chronic toxicity (6 months) oral doses of 2 mg (therapeutic dose human), 5 mg and 10 mg Fe / kg per day were also conducted in rats.

None of the hematology laboratory studies have revealed no signs of damage in experimental animals, which could be attributed to the substance under investigation. Hematocrit, hemoglobin, red blood cells and white blood cells remained constant in the test period (Hausmann and Mueller, 1984).

Histopathologic studies were performed in animals that received 10 mg iron/kg per day and all the control animals. In the gastrointestinal tract did not reveal changes in the mucous or signs of erosion, inflammation, ulcers or bleeding. Only in the spleen were noted little change. In female rats were observed deposits of iron-containing pigment (more pronounced and the size and number). It is equally frequently detected in treated as well as in non-treated groups of animals.

Genotoxicity:

Not detected mutagenic activity of Iron Polymaltose Complex during cytogenetic tests in vitro. Mutagenic potential of Iron Polymaltose Complex were studied in a culture of human lymphocytes in vitro (Adams, 1996).

Iron Polymaltose Complex, regardless of the dose did not produce statistically significant increase in metaphase loops containing chromosomal aberrations, both in the presence and absence of S-9 mix, compared with a control solution.

All the substances that make up the group of positive control, namely mitomycin C and cyclophosphamide induced a statistically significant increase in the proportion of aberrant cells.

Carcinogenicity:

A number of studies have shown that supplementary iron added to the diet enhances the development of neoplasia in animals that produce spontaneous tumors, are inoculated with tumor cells, or are exposed to chemical carcinogens. However, high-level (1200 – 1500 mg/kg bw/day) dietary carbonyl iron supplementation had no effect on the initiation or promotion of hepatocarcinoma in the Solt-Farber model of hepatocarcinogenesis in rats.

Reproductive and developmental toxicity:

A multigenerational study in rats showed no adverse effects of 20 mg/kg bw/week maternal iron supplementation (by intramuscular injection, but not during pregnancy) on the numbers of offspring produced or their growth weights, with no significant evidence of excess iron transfer across the placenta. A study of maternal iron poisoning in an ovine model also showed that extremely elevated maternal serum iron concentrations were not accompanied by corresponding increases in fetal serum iron levels.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Hydroxide.

Sodium Chloride.

Water for Injection.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years

6.4 Special precautions for storage

Store at temperature not exceeding 30°C, in original package.

6.5 Nature and contents of container

Carton box containing an opaque plastic drawer (of 3 amber ampoules) and a pamphlet.

6.6 Special precautions for disposal

Not special requirements.

7. MARKETING AUTHORISATION HOLDER

EUROPEAN EGYPTIAN PHARM. IND.

Alexandria-Cairo Desert Road Km 25,

Alexandria,

Egypt.

8. MARKETING AUTHORISATION NUMBER(S)

22949/2014.

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

30/10/2014.

10. DATE OF REVISION OF THE TEXT

May 2023.