SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF MEDICINAL PRODUCT

EMFER 100 mg/5 ml IV Ampoule

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient:

Each ampoule (5 ml) contains complex of iron hydroxide sucrose equivalents to 100.0 mg (20 mg/ml) iron (III).

Excipient(s):

Sodium hydroxide

For excipients, refer to 6.1.

3. PHARMACEUTICAL FORM

Ampoule

Brown, homogen solution.

4. CLINICAL PROPERTIES

4.1 Therapeutic indications

EMFER is indicated for anemia of iron insufficiencies for following conditions:

- Clinical requirements of rapidly providing iron to iron stores,
- In patients with intolerated to oral iron preperations or in patient with showing non-conformity to oral iron preperations.
- In active inflamatory colon disease which oral iron preperations are ineffective.

Diagnosis of iron insufficiency must support with suitable laboratory tests (exp; serum ferritin, serum iron, saturation of transferring and hypocramia of red blood cells).

4.2 Posology and method of administration

Posology:

Total dosage is 100 mg not more than 3 per week. According to clinic condition, dosage can increase 200 mg as maximum 3 times per week. Required total dosage increase than maximum single dosage, usage must hafway down.

Total cumulative dosage of EMFER equivalents to total iron insufficiency depending on hemoglobin level and body weight (mg). Dosage of EMFER must calculate with below formula according to total iron insufficiency.

Total iron insufficiency (mg) =
Body weight [kg] x (Desired hemoglobin – measured hemoglobin)[g/] x 0.24* + stored iron [mg]

Until 35 kg body weight =
Desired hemoglobin: 130 g/l and stored iron: 15 mg/kg body weigth

35 kg and more than 35 kg body weight =
Desired hemoglobin: 150 g/l and stored iron: 500 mg

*Factor 0.24= 0.0034 x 0.07 x 1000 (iron content of hemoglobin 0.34%; ratio of blood volume to body weight 0.7%; Factor 1000 = Changing factor of g to mg)

Required EMFER quantity is determined with above calculation or below dosage table:

Body weight (kg)	**Admistered numbers of EMFER ampoules**			
	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

For changing of Hb (mM) to Hb (g/l), multiply with 16.1145.

Administration frequecy and time:
Total dosage of iron sucrose injection, adminster not more than 3 per week as single dosage. Treatment must continue until providing iron needing.

Administration route:
EMFER must administer only by intravenously. This administration must by slow intravenous injection or intravenous drop infusion. Before strating treatment with EMFER, test dosage must be given to patient before administration of first dosage for each patient.

EMFER must not use by intramuscular or subcutane injection.

Intravenous drop infusion:
EMFER is diluted only with 0.9% sodium chloride solution. 5 ml EMFER ampoule (100 mg iron) is diluted with maximum 100 ml steril 0.9% sodium chloride solution. 10 ml EMFER ampoule (200 mg iron) is diluted with maximum 200 ml sterile 0.9% sodium chloride solution. More lower concentrations of EMFER are not preferred in point of view stability.

First 25 mg iron (25 ml solution) must adminster by infusion for first 15 minutes as test dosage. Within this timing, if you have been not noticed any side effects, remaining parts of infusion administer as maximum 50 ml within 15 minutes.

- 100 mg iron (5 ml EMFER) minimum for 15 minutes
- 200 mg iron (10 ml EMFER) minimum for 30 minutes

Intravenous injection:
EMFER is administered by slow intravenous injection of 1 ml un-diluted solution per minute (5 minutes for each ampoule) and not more than 2 ampoule of EMFER (200 mg iron) for each injection.

Before administration of slow intravenous injection 1 ml (20 mg iron) test dosage must be administer slowly for 1-2 minutes. After completing of test dosage, if you have not seen any un-wanted reactions within 15 minutes, remaining part of injection can administer.

Injection with dialysis machine:
EMFER is administer into venous sytem of dialysis machine towards to middle of hemodialysis seance according to procedures mentioned in intravenous applications.

Additional information related to special populations:

Renal insufficiency:
Total dosage for hemodyalised patients is 1000 mg administered by 10 dosages. If it is necessary, recommended dosage can repeat. Dosage administration frequency must not more than 3 per week.

Liver insufficiency:
In patients with liver insufficiency, it must use after risk/benefit evaluations in case of absolute necessity.

Pediatric populations:
Because of no data related to safety and efficacy in pediatric populations, EMFER usage is not proposed.

Geriatric populations:
EMFER must use in geriatric populations as mentioned in section of "Posology/administration frequency and time".

4.3 Concentradications

EMFER usage in concentracated for following conditions:

- In patients with knowing hypersensivity to EMFER or excipients in its content,
- Anemia not related to iron insufficiency,
- Excess of iron or defeating of iron usage,
- In patients with astma, egzema or other atopic allergies because of sensivity to allergic reactions,
- In pregnant within first trimaster of pregnancy.

4.4 Special precautions and warnings

Parenterally administered iron preperations can cause allergic or anaphyloctoid reactions causing death. Because of this, cardio-pumonary recucitation equipments must availible and ready for usage.

In patients with liver disfunctions, parenteral iron must adminster only after risk/benefit evaluations carefully. In patients with hepatic disfunction, usage of Porfiria Cutenea Tarda (PCT) must avoided because it is precipitating factor for excess iron loading. For preventing of excess iron, iron conditions must monitör carefully.

Parenteral iron must use carefully in case of acute or chronic infections. In case of countinuing bacteriaemia, stopping of iron sucrose usage is recommended. In patients with chronic infections, risk/benefit evaluations must perform thinking of erytropoesis suppression.

In rapid administration of injection, hypotension can occur. Sometimes allergic reactions including artralgia are seen in case of excessing recommended dosages.

Flowing in near or surrounding of vens must avoided. Because EMFER flowing in injection site can cause pain, inflamation, tissue necrose and browning of skin.

Wrongly administration of iron preperations to under 6 years of ages- children can cause fetal poisinings. Because of this, this medicines store at places not to reach or not to see for children.

This medicine contains less than 1 mmol (23 mg) sodium in each dosage, so it is exactly no contains sodium.

4.5 Interactions with other medicines and types of other interactions

Like other parenteral iron preperations, when EMFER ampoule is used with oral iron preperations, oral iron absorbtion can decrease. Because of this, oral iron treatment must start after minimum 5 days from last injection of EMFER.

Additional information related to special populations:

Any interaction studies are not conducted related to special populations.

4.6 Pregnancy and lactation

General recommendation

Pregnancy category: B

Womens with child bearing potential/ contraception

For EMFER, clinical data related to exposing to pregnants.

Studies conducted in animals do not show harmfull effects directly or in-drectly related to development after birth or pregnancy/ embrional/fetal development/ birth (refer to 5.3).

When administration to pregnant women, precautions must taken.

Pregnancy period

Limited data related to exposing in pregnancy do not show advesr effects on fetus/ newborns or pregnancy. Any epidemiological data are not obtained until to date.

Lactation period

It is not known that whether iron hydroxide sucrose complex is excreted by human milk or not. Cunducted animal studies do not show excreting of iron hydroxide sucrose complex by milk. When deciding of stopping lactation or stopping of EMFER treatment, benefits of lactating for children or benefits of EMFER treatment to lactating woman must think of carefully.

Reproducing ability/fertility

There is no known effects of reproducing ability.

4.7 Effects of driving and usage of machinery

After administration of EMFER, dazing, confusion or dizzeness can seen and patients must avoided from driving and usage machinary until resolving of symptoms.

4.8 Advers Events

Advers events are listed according to system organ class and frequecy like this:

Very common (≥ 1/10), common (≥ 1/100 -≤ 1/10), non-common (≥ 1/1.000 - ≤ 1/100), rare (≥ 1/10.000 - ≤ 1/1.000) and very rare (≤ 1/10.000), not known (not estimated from availible data).

Immun system disorders

Rare: Anaphlactoid reactions (rarely including artralgia), urticaria

Nervous system disorders

Common:	Cahanging of tasting (specially metalic taste)
Non-common:	Dazing, headache
Rare:	Paraestesia

Cardiovascular disease

Non-common: Hypotension and collapse, tachicardia and palpitations

Respiration, chest disease and mediastinal disease
Non-common: Broncospasm, dispnea

Gastrointestinal disease
Non-common: Nausea, vomiting, abdominal pain, diarreae

Skin and sub-skin tissue disorders
Non-common: Pruritis, urticaria, exantema, erytema

Muscle-skeleton disease, connective tissue and bone disease
Non-common: Muscle cramps, myalgia

Genral disorders and disorders related to injection site
Non-common: Fever, shivering, redness, erythema, chest pain, burming at injection site, tightness
Rare: Peripheral oedema, tiredness, astenia, malaysia, indisposition.
Isolated cases: Decreasing of memmory level, dazedness, confusion, angiooedema, decreasing attention, back pain.

4.9 Overdosages and treatment

Overdosages with EMFER cause hemocyderosis because of excess iron loading. For diagnosis of mentioned table, serum ferritin level and transferrin saturation must monitör periodically.

In case of overdosage of EMFER or very rapid administration of injection, symptoms like hypotension, headache, vomiting, nausea, diarrea, abdominal pain, dizziness, joint pains, paraestesia, muscle pain, oedema, dispnea, urticaria, chest pain and cardiovascular collapse are seen.

Overdosage can treat with supportive measurements and if necessary with clating agent treatment which is iron binder. Most of syptoms treat with liquid by intravenoulsly, hydrocortisone and/or antihitaminics. It is not removed from body by dialysis.

In case of overdosages, despherroxamine (in children: by I.V. as 15 mg/kg/hour; in adults by I.V. at starting dosage of 1000 mg, after 500 mg until next two dosage for each 4 hours) or calcium disodium EDTA (by I.M. as 167 mg/m^2 for each 4 hours; by I.V. as infusion of 8-24 hours or 1 g/m^2 for each 12 hours divided to 1) usages are recommended. Despherroxamine has got teratogenic effects.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

ATC code: B03AC02
Pharmacotherapeutical group: Threevalane iron preperations

Normal eritropoesis is depending on iron in plasma and concentration of erytropoeietin. After IV administration of iron sucrose, comparisonal changing ocuurs between iron (III) hydroxide complex and transferrine which is iron binding protein. Therapeutical response to iron treatment is depending on conditions of iron stores for patients and usage ability of iron. İron usage is influenced by reason of iron insufficiency and other disease influencing normal erytropoesis. Protein energy malnutrition prevents joiningof iron in erytrocytes independently from stored iron quantities. Single iron treatment is not increasing quantities of erythrocytes. İron treatments is healing only anemia related iron insufficiency.

Using marked ^{59}Fe ve ^{52}Fe, iron cinetical studies are performed in 5 patients with anemia and chronic renal function. Plasma clirens of ^{52}Fe are between 60-100 minutes. ^{52}Fe is distributed into liver, spleen and bone morrow. After 2 weeks from administration, usage ratio of ^{59}Fe by erythocytes are between 62%-97%.

Complex of iron (III) hydroxide sucrose is brown-reddish powder. It dissolves in water freely.

5.2 Pharmacokinetical properties

Genral properties

Absorbtion:
With regard to application route, medicine (intravenous) is directly enter to blood.

Distribution:
After administration of 100 mg iron by intravenous injections in healty volunteers, maxium iron levels are reached for 10 minutes later for injection with average value of 538 µ mole/L. Central distrubution volume is conforming to directly plasma volume (approximately 3 liters). Injected iron is rapidly cleared from plasma. Half life is approximately 6 hours. Distribution volume is approximately 8 liters in stabile conditions. When comparing with transfferin, stability of iron sucrose is very low and because of this it shows verylow distrubution in body liquids. As result of this, iron transferring is approximately 31 mg iron /24 hours.

Biotransformation:
It is seperated to iron and sucrose in reticuloendotelial system.

Elimination:
Renal elimination of iron is lower than 5% of total body clearance for first 4 hours after injection. After 24 hours, plasma iron level descreases to levels before injection and approximately 75% dosage of iron sucrose is eliminated. Elimination half life is 6 hours in healthy adults.

Linearity/non-linearity condition:
Not availible.

Characteristic properties in patients

Renal /liver insufficiencies:

There is no information related to pharmacological properties in patients with renal and liver insufficiencies.

5.3.Pre-clinical safety data
There is no enough data related to pre-clinical safety data.

6. PHARMACEUTICAL PROPERTIES

6.1 List of excipients
Sodium hydroxide
Water for injection

6.2 Incompabilities
EMFER must mixed with only 0.9% sodium chloride. Other dilution solution or infusion solution do not use. These solutions can cause precipitations with other therapeutic agents and/or interactions. As packaging materials, incompabilities of PE or PVC except for glass are not known.

6.3 Shelf-life
36 months
Shelf-life after first opening: Microbiological point of view product must use immediately after opening.
Shelf-life after dilution with 0.9% sodium chloride: Microbiological point of view, product must use immediately. Prepared solution must administer to patient as contained 100 mg iron in minimum 15 minutes.

6.4 Precautions for storage
Store at below 25°C room temperature.
Do not freeze.

6.5 Nature and content of packaging

EMFER 100 mg/5 ml IV ampoule is presented in boxes containing 5 ml of 5 ampoules.

6.6 Discarding of remaining parts of products and other special methods
Unused products or discarded materials must discard according to guidelines of controlling of medicinal products and controlling of packaging and packaging garbages.

Precipitations can occur in case of nonsuitable storages. Ampoules must visually contol in point of view for precipitations and degredation before usage. Diluted solution must be brown and clear. Expiry dated or ampoules with precipitations must not use.

7 REGISTRATION HOLDER
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8 REGISTRATION NUMBER(S)

254/3

9 FIRST REGISTRATION DATE /RENEWAL DATE

First Registration Date:
Renewal date of registration:

10 RENEWAL DATE OF SMPC