FERRASIL®
Iron sucrose
Solution for intravenous use

Arwan

Composition
Each 5 ml ampoule contains:
Active ingredient: 20 mg/ml iron as iron sucrose corresponding to 100 mg iron per ampoule.
Excipients: Sodium hydroxide and water for injection.

Indications
Ferrasil is indicated for the treatment of iron deficiency in the following indications:
- where there is a clinical need to deliver iron rapidly to iron stores,
- in patients who cannot tolerate oral iron therapy or who are non-compliant,
- In active inflammatory bowel disease where oral iron preparations are ineffective.

The diagnosis of iron deficiency must be based on appropriate laboratory tests (e.g. Hb, serum ferritin, serum iron, etc.).

Dosage and administration
Dosage
Calculation of dosage:

The dose for **Ferrasil** must be individually determined for each patient 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] x 0.24* + depot iron [mg]

- Below 35 kg body weight: target Hb = 130 g/l and depot iron = 15 mg/kg body weight
- 35 kg body weight and above: target Hb = 150 g/l and depot iron = 500 mg

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

The total amount of **Ferrasil** required in mg is determined from above calculation. Alternatively, the total amount of **Ferrasil** required in ml is determined from the following formula or dosage table.

$$\text{Total amount of Ferrasil required [ml]} = \frac{\text{Total iron deficit [mg]}}{\text{20 mg/ml}}$$

Body Weight [kg]	Total number of ampoules Ferrasil to be administered (1 ampoule of Ferrasil corresponds to 5 ml)			
	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

To convert Hb (mM) to Hb (g/l), multiply the former by 16.1145

Adults and the elderly: The total cumulative dose of **Ferrasil**, equivalent to the total iron deficit (mg), is determined by the haemoglobin level and body weight (see Calculation of dosage).
The normal posology is 5-10 ml of **Ferrasil** (100-200 mg) once to three times a week.
The total single dose must not exceed 200 mg of iron given not more than three times per week. If the total necessary dose exceeds the maximum allowed single dose, then the administration has to be split.
Children: Its use has not been adequately studied in children and, therefore, it is not recommended for use in children.

Administration
Ferrasil must only be administered by intravenous route. This may be by a slow intravenous injection or by an intravenous drip infusion. Before administering the first dose to a new patient, a test dose of **Ferrasil** should be given.
Ferrasil must not be used for intramuscular injection.
Intravenous drip infusion: **Ferrasil** must be diluted only in sterile 0.9% w/V sodium chloride solution:
- 5 ml **Ferrasil** (100 mg iron): in maximum 100 ml sterile 0.9% m/V sodium chloride solution.
- 10 ml **Ferrasil** (200 mg iron): in maximum 200 ml sterile 0.9% m/V sodium chloride solution.

For stability reasons, dilutions to lower **Ferrasil** concentrations are not permissible.
Dilution must take place immediately prior to infusion and the solution should be administered as follows:
- 100 mg iron (5 ml **Ferrasil**) in at least 15 minutes.
- 200 mg iron (10 ml **Ferrasil**) in at least 30 minutes.

The first 25 mg of iron (i.e. 25 ml of solution) should be infused as a test dose over a period of 15 minutes. If no adverse reactions occur during this time then the remaining portion of the infusion should be given at an infusion rate of not more than 50 ml in 15 minutes.
Intravenous injection: **Ferrasil** may be administered by slow intravenous injection at a rate of 1 ml undiluted solution per minute (i.e. 5 minutes per ampoule) and not exceeding 10 ml **Ferrasil** (200 mg iron) per injection.
Before administering a slow intravenous injection, a test dose of 1 ml (20 mg of iron) should be injected slowly over a period of 1 to 2 minutes. If no adverse events occur within 15 minutes of completing the test dose, then the remaining portion of the injection may be given.
Injection into dialyser: **Ferrasil** may be administered during a haemodialysis session directly into the venous limb of the dialyser under the same procedures as those outlined for intravenous injection.

Contraindications
The use of **Ferrasil** is contraindicated in cases of:
- known hypersensitivity to any of its components,
- anaemia not attributable to iron deficiency,
- iron overload or disturbances in utilization of iron,
- patients with a history of asthma, eczema or other atopic allergy, because they are more susceptible to experience allergic reactions,
- pregnancy first trimester.

Warnings and precautions
Parenterally administered iron preparations can cause allergic or anaphylactoid reactions, which may be potentially fatal. Therefore, treatment for serious allergic reactions and facilities with the established cardio-pulmonary resuscitation procedures should be available.
In patients with liver dysfunction, parenteral iron should only be administered after careful risk/benefit assessment. Parenteral iron administration should be avoided in patients with hepatic dysfunction where iron overload is a precipitating factor, in particular Porphyria Cutanea Tarda (PCT). Careful monitoring of iron status is recommended to avoid iron overload.
Parenteral iron must be used with caution in case of acute or chronic infection. It is recommended that the administration of iron sucrose is stopped in patients with ongoing bacteraemia. In patients with chronic infection a risk/benefit evaluation has to be performed, taking into account the suppression of erythropoiesis.
Hypotensive episodes may occur if the injection is administered too rapidly. Allergic reactions, sometimes involving arthralgia, have been more commonly observed when the recommended dose is exceeded.
Paravenous leakage must be avoided because leakage of **Ferrasil** at the injection site may lead to pain, inflammation, tissue necrosis and brown discoloration of the skin.

Pregnancy and lactation
Pregnancy: Data on a limited number of exposed pregnancies indicated no adverse effects of **Ferrasil** on pregnancy or on the health of the foetus/newborn child. No well-controlled studies in pregnant women are available to date. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development.
Nevertheless, risk/benefit evaluation is required.
Ferrasil should only be used in pregnant women in whom oral iron is ineffective or cannot be tolerated and the level of anaemia is judged sufficient to put the mother or foetus at risk.
Pregnancy first trimester: see contraindications.
Lactation: Non metabolised **Ferrasil** is unlikely to pass into the mother's milk. No well-controlled clinical studies are available to date. Animal studies do not indicate direct or indirect harmful effects to the nursing child.

Driving and using machines
It is unlikely that **Ferrasil** has an influence on the ability to drive and use machines.
In the case of symptoms of dizziness, confusion or light headedness following the administration of **Ferrasil**, patients should not drive or use machinery until the symptoms have ceased.

Undesirable effects
The most frequently reported adverse drug reactions of iron sucrose in clinical trials were transient taste perversion, hypotension, fever and shivering, injection site reactions and nausea, occurring in 0.5 to 1.5% of the patients. Non-serious anaphylactoid reactions occurred rarely.
In general anaphylactoid reactions are potentially the most serious adverse reactions (see "Warnings and precautions").
In clinical trials, the following adverse drug reactions have been reported in temporal relationship with the administration of **Ferrasil**, with at least a possible causal relationship: Common: (≥1/100, <1/10), uncommon (≥1/1000, <1/100), rare (≥1/10000, <1/1000).
Nervous system disorders: Common: transient taste perversions (in particular metallic taste). Uncommon: headache, dizziness. Rare: paraesthesia, syncope, loss of consciousness, burning sensation.
Cardio-vascular disorders: Uncommon: Hypotension and collapse, tachycardia and palpitations. Rare: hypertension.
Respiratory, thoracic and mediastinal disorders: Uncommon: bronchospasm, dyspnoea.
Gastrointestinal disorders: Uncommon: nausea, vomiting, abdominal pain, diarrhoea.
Skin and subcutaneous tissue disorders: Uncommon: pruritus, urticaria, rash, exanthema, erythema.
Musculoskeletal, connective tissue and bone disorders: Uncommon: muscle cramps, myalgia.
General disorders and administration site disorders: Uncommon: fever, shivering, flushing, chest pain and tightness. Injection site disorders such as superficial phlebitis, burning, swelling. Rare: anaphylactoid reaction (rarely involving arthralgia), peripheral oedema, fatigue, asthenia, malaise, feeling hot, oedema.
Immune system disorders: Rare: anaphylactoid reactions.
Moreover, in spontaneous reports the following adverse reactions have been reported:
Isolated cases: reduced level of consciousness, light-headed feeling, confusion, angio-oedema, swelling of joints, hyperhidrosis, back pain, bradycardia, chromaturia.

Overdosage
Overdosage can cause acute iron overloading which may manifest it-self as haemosiderosis. Overdosage should be treated with supportive measures and, if required, an iron chelating agent.

Interactions
As with all parenteral iron preparations, **Ferrasil** should not be administrated concomitantly with oral iron preparations since the absorption of oral iron is reduced. Therefore an oral iron therapy should at least be started 5 days after the last injection.

Revision date: May 2014

Pharmacodynamics

The ferrokinetics of iron sucrose labeled with ^{59}Fe and ^{59}Fe were assessed in 5 patients with anaemia and chronic renal failure. Plasma clearance of ^{52}Fe was in the range of 60 to 100 minutes. ^{52}Fe was distributed to the liver, spleen and bone marrow. At two weeks after administration, the maximum red blood cell utilization of ^{59}Fe ranged from 62% to 97%.

Pharmacokinetics

Following intravenous injection of a single dose of **Ferrasil** containing 100 mg iron in healthy volunteers, maximum iron levels, averaging 538 µmol/l, were obtained 10 min after injection. The volume of distribution of the central compartment corresponded well to the volume of plasma (approx. 3 litres).

The iron injected was rapidly cleared from the plasma, the terminal half-life being approx. 6 h. The volume of distribution at steady state was about 8 litres, indicating a low iron distribution in the body fluid. Due to the lower stability of iron sucrose in comparison to transferrin, a competitive exchange of iron to transferrin was observed. This resulted in iron transport of approx. 31 mg iron/24 h.

Renal elimination of iron, occurring in the first 4 h after injection, corresponds to less than 5% of the total body clearance. After 24 h the plasma levels of iron were reduced to the pre-dose iron level and about 75% of the dosage of sucrose was excreted.

Incompatibilities

Ferrasil must only be mixed with 0.9% w/v NaCl solution. No other solutions and therapeutic agent should be used as there is potential of precipitation and/or interaction. The compatibility with containers other than glass, polyethylene and PVC is not known.

Shelf life

Shelf life after first opening of the container:

From a microbiological point of view, the product should be used immediately.

Shelf life after dilution with sterile 0.9% m/V sodium chloride solution:

From a microbiological point of view, the product should be used immediately after dilution with sterile 0.9% m/V sodium chloride solution.

Special precautions for disposal and other handling

Ampoules should be visually inspected for sediment and damage before use. Only those with sediment free and homogenous solution must be used.

The diluted solution must appear as brown and clear.

Any unused product or waste material should be disposed of in accordance with local requirements.

From a microbiological point of view, the product should be used immediately after dilution with sterile 0.9% m/V sodium chloride solution.

Expiry date and storage conditions

See the expiry date printed on the outer carton.

This date refers to the product correctly stored in unopened package.

Beware not to use **Ferrasil** after this date.

Store below 25°C. Do not freeze.

Keep all medicines out of reach of children.

Any unused product or waste material should be disposed of in accordance with local requirements.

From a microbiological point of view, the product should be used immediately after dilution with sterile 0.9% m/V sodium chloride solution.

Presentation

Ferrasil is a dark brown, non transparent, aqueous solution.

Ferrasil solution for intravenous use is available in packs of 5 ampoules (each of 5 ml solution).

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THIS IS A MEDICAMENT

- 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 medicines, their 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.
- Keep all medicaments out of the reach of children.

Council of Arab Health Ministers, Union of Arab Pharmacists