

SUMMARY OF PRODUCT CHARACTERISTICS

- ▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

FERINJECT 50 mg iron/ml solution for injection/infusion.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml of solution contains ferric carboxymaltose corresponding to 50 g of iron.

One 10 ml vial contains ferric carboxymaltose corresponding to 500 mg of iron.

Sodium hydroxide is added as excipient for pH adjustment. Therefore one milliliter of solution contains up to 5.5 mg (0.24 mmol) sodium, see section 4.2. For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for intravenous administration.

Dark brown, non-transparent, aqueous solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Iron deficiency in patients in whom oral iron therapy is not sufficiently effective, is ineffective or cannot be undertaken, such as cases where oral iron preparations cannot be tolerated or in the presence of inflammatory gastrointestinal diseases, e.g. ulcerative colitis, which may be exacerbated by oral iron therapy, or in the case of treatment-refractory iron-deficiency states where it is suspected that the oral iron preparations are being taken unreliably. Ferinject should only be administered if the diagnosis of iron deficiency has been established and confirmed through appropriate laboratory investigations (e.g. plasma ferritin levels transferrin saturation (TSAT), haemoglobin, haematocrit, red cell count, MCV and MCH).

4.2 Posology and method of administration

Monitor carefully patients for signs and symptoms of hypersensitivity reactions during and following each administration of Ferinject.

Ferinject should only be administered when staff trained to evaluate and manage anaphylactic reactions is immediately available, in an environment where full resuscitation facilities can be assured. The patient should be observed for adverse effects for at least 30 minutes following each Ferinject administration (see section 4.4).

Posology

The posology of Ferinject follows a stepwise approach: [1] determination of the individual iron need, [2] calculation and administration of the iron dose(s), and [3] post-iron repletion assessments. These steps are outlined below:

Step 1: Determination of the iron need

The individual iron need for repletion using Ferinject is determined based on the patient's body weight and haemoglobin (Hb) level. Refer to Table 1 for determination of the iron need:

Table 1: Determination of the iron need

Hb		Patient body weight		
g/dL	mmol/L	below 35 kg	35 kg to <70 kg	70 kg and above
<10	<6.2	500 mg	1,500 mg	2,000 mg
10 to <14	6.2 to <8.7	500 mg	1,000 mg	1,500 mg
≥14	≥8.7	500 mg	500 mg	500 mg

Iron deficiency must be confirmed by laboratory tests as stated in 4.1.

Step 2: Calculation and administration of the maximum individual iron dose(s)

Based on the iron need determined above the appropriate dose(s) of Ferinject should be administered taking into consideration the following:

A single Ferinject administration should not exceed:

- 15 mg iron/kg body weight (for administration by intravenous injection) or 20 mg iron/kg body weight (for administration by intravenous infusion)
- 1,000 mg of iron (20 mL Ferinject)

The maximum recommended cumulative dose of Ferinject is 1,000 mg of iron (20 mL Ferinject) per week.

Step 3: Post-iron repletion assessments

Re-assessment should be performed by the clinician based on the individual patient's condition. The Hb level should be re-assessed no earlier than 4 weeks post final Ferinject administration to allow adequate time for erythropoiesis and iron utilisation. In the event the patient requires further iron repletion, the iron need should be recalculated using Table 1 above. (See section 5.1.)

Special Population – patients with haemodialysis-dependent chronic kidney disease

A single maximum daily dose of 200 mg iron should not be exceeded in haemodialysis-dependent chronic kidney disease patients (see also section 4.4).

Paediatric population

The use of Ferinject has not been studied in children, and therefore is not recommended in children under 14 years.

Method of administration

Ferinject must only be administered by the intravenous route:

- by injection, or
- by infusion, or
- during a haemodialysis session undiluted directly into the venous limb of the dialyser.

Ferinject must not be administered by the subcutaneous or intramuscular route.

Intravenous injection

Ferinject may be administered by intravenous injection using undiluted solution. The maximum single dose is 15 mg iron/kg body weight but should not exceed 1,000 mg iron. The administration rates are as shown in Table 2:

Table 2: Administration rates for intravenous injection of Ferinject

Volume of Ferinject required			Equivalent iron dose			Administration rate / Minimum administration time
2	to	4 mL	100	to	200 mg	No minimal prescribed time
>4	to	10 mL	>200	to	500 mg	100 mg iron / min
>10	to	20 mL	>500	to	1,000 mg	15 minutes

Intravenous infusion

Ferinject may be administered by intravenous infusion, in which case it must be diluted. The maximum single dose is 20 mg iron/kg body weight, but should not exceed 1,000 mg iron.

For infusion, Ferinject must only be diluted in sterile 0.9% m/V sodium chloride solution as shown in Table 3. Note: for stability reasons, Ferinject should not be diluted to concentrations less than 2 mg iron/mL (not including the volume of the ferric carboxymaltose solution). For further instructions on dilution of the medicinal product before administration, see section 6.6.

Table 3: Dilution plan of Ferinject for intravenous infusion

Volume of Ferinject required			Equivalent iron dose			Maximum amount of sterile 0.9% m/V sodium chloride solution	Minimum administration time
2	to	4 mL	100	to	200 mg	50 mL	No minimal prescribed time
>4	to	10 mL	>200	to	500 mg	100 mL	6 minutes
>10	to	20 mL	>500	to	1,000 mg	250 mL	15 minutes

4.3 Contraindications

The use of Ferinject is contraindicated in cases of:

- hypersensitivity to the active substance, to Ferinject or any of its excipients listed in section 6.1.
- known serious hypersensitivity to other parenteral iron products.
- anaemia not attributed to iron deficiency, e.g. other microcytic anaemia.
- evidence of iron overload or disturbances in the utilisation of iron.

4.4 Special warnings and precautions for use

Hypersensitivity reactions

The intravenous administration of parenteral iron products can cause immediate-type acute hypersensitivity reactions (anaphylactoid/anaphylactic reactions), including anaphylactoid reactions which may be fatal.

Such reactions have been reported even where previous administrations of parenteral iron products have been tolerated without complications. There are reports of hypersensitivity reactions that can progress to Kounis syndrome (acute allergic spasm of the coronary arteries that can result in myocardial infarction). Treatment with Ferinject should be prescribed by the attendant physician only after carefully determining the indication.

Ferinject should only be used if healthcare professionals who can assess and treat anaphylactic reactions are immediately available as well as only in an institution in which all facilities for resuscitation are available. Before each administration of Ferinject, patients should be actively questioned about previous adverse reactions to intravenous iron products.

Typical symptoms of acute hypersensitivity reactions are: fall in blood pressure, tachycardia (and even anaphylactic shock), respiratory symptoms (including bronchial obstructions, laryngeal and pharyngeal oedema), abdominal symptoms (including abdominal cramps, vomiting) or skin symptoms (including urticaria, erythema, pruritus).

Patients should be carefully monitored for any signs and symptoms of a hypersensitivity reaction during and for at least 30 minutes after the administration of parenteral iron products. Should allergic reactions or signs of intolerance occur during administration, the treatment must be stopped immediately.

Adrenaline, e.g. in doses of 0.3 mg intramuscularly, is recommended in the first instance for the emergency drug treatment of acute anaphylactic/anaphylactoid reactions, and only after this antihistamines and/or corticosteroids (later onset of action).

In rare cases, fever or delayed allergic reactions (with a delay of several hours or even days) have been observed.

The risk of hypersensitivity reactions is increased in patients with known allergies including drug intolerance, a history of severe asthma, eczema and other forms of atopy, and also in patients with immunological or inflammatory disorders (e.g. systemic lupus erythematosus, rheumatoid arthritis).

Hypophosphataemia/hypophosphataemic osteomalacia

Parenteral iron can lead to hypophosphataemia, which is transient and without clinical symptoms in most cases. Hypophosphatemia requiring treatment has mainly been reported in individual cases, in patients with known risk factors and after sustained higher dosing.

Cases of symptomatic hypophosphataemia leading to hypophosphataemic osteomalacia, and fractures requiring clinical intervention, including surgery, were reported after market introduction. In case of arthralgia or bone pain, patients should be advised to seek medical advice.

Patients receiving multiple higher doses as part of long-term treatment, and who have underlying risk factors (e.g. vitamin D deficiency, calcium and phosphate malabsorption, secondary hyperparathyroidism, hereditary haemorrhagic telangiectasia, inflammatory bowel disease and osteoporosis) should be monitored for hypophosphataemic osteomalacia, including serum phosphate control. In case of persistent hypophosphataemia, treatment with Ferinject should be re-evaluated.

Hepatic or renal insufficiency

Parenteral iron should only be administered to patients with hepatic dysfunction following a careful assessment of the risks and benefits.

Parenteral iron administration should be avoided in patients with hepatic dysfunction due to iron overload, especially those with porphyria cutanea tarda, or any acute liver disease.

Careful monitoring of the iron status is recommended to avoid iron overload.

Infections

Parenteral iron should be administered with caution in cases of acute or chronic infections, asthma, eczema or atopic allergies.

In the case of patients with bacteraemia, it is recommended to stop administration of Ferinject.

Extravasation

Paravenous administration should be avoided. It may irritate the skin and potentially cause a long-lasting, brownish discolouration on the injection/infusion site. The administration of Ferinject must be discontinued immediately if this occurs.

Other ingredients

One ml of Ferinject may contain up to 5.5 mg (0.24 mmol) of sodium. This must be taken into account when administering to people on a sodium-controlled diet.

4.5 Interaction with other medicinal products and other forms of interaction

Ferinject should not be administered concomitantly with oral iron preparations since the absorption of oral iron can be reduced.

See also section “4.1 Therapeutic indications”

4.6 Fertility, pregnancy and lactation

Pregnancy:

There are limited data from the use of Ferinject in pregnant women (see section 5.1). A careful benefit/risk evaluation is required before use during pregnancy and Ferinject should not be used during pregnancy unless clearly necessary.

Iron deficiency occurring in the first trimester of pregnancy can in many cases be treated with oral iron. Treatment with Ferinject should be confined to the second and third trimester if the benefit is judged to outweigh the potential risk for both the mother and the foetus.

Foetal bradycardia may occur following administration of parenteral irons. It is usually transient and a consequence of a hypersensitivity reaction in the mother. The unborn baby should be carefully monitored during intravenous administration of parenteral irons to pregnant women.

Animal data suggest that iron released from Ferinject can cross the placental barrier and that its use during pregnancy may influence skeletal development in the fetus (see section 5.3).

Breast feeding:

Clinical studies showed that transfer of iron from Ferinject to human milk was negligible ($\leq 1\%$). Based on limited data on breast-feeding women it is unlikely that Ferinject represents a risk to the breast-fed child.

Fertility:

There are no data on the effect of Ferinject on human fertility. Fertility was unaffected following Ferinject treatment in animal studies (see section 5.3).

4.7 Effects on ability to drive and use machines

No relevant studies have been performed. It is unlikely that Ferinject has an effect on the ability to drive and use machines.

4.8 Undesirable effects

Table 4 presents the adverse drug reactions (ADRs) reported during clinical studies in which > 8,000 subjects received Ferinject, as well as those reported from the post-marketing experience (see table footnotes for details).

The most commonly reported ADR is nausea (occurring in 2.9% of the subjects), followed by injection/infusion site reactions, hypophosphataemia, headache, flushing, dizziness and hypertension. Injection/infusion site reactions comprise several ADRs which individually are either uncommon or rare. The most serious ADR is anaphylactoid/anaphylactic reactions (rare); fatalities have been reported. See section 4.4 for further details.

Table 4: Adverse drug reactions observed during clinical trials and post-marketing experience

System Organ Class	Common ($\geq 1/100$ to $< 1/10$)	Uncommon ($\geq 1/1,000$ to $< 1/100$)	Rare ($\geq 1/10,000$ to $< 1/1,000$)	Frequency not known⁽¹⁾
Immune system disorders		Hypersensitivity	Anaphylactoid/ anaphylactic reactions	
Metabolism and nutritional disorders	Hypophosphataemia			

Nervous system disorders	Headache, dizziness	Paraesthesia, dysgeusia		Loss of consciousness ⁽¹⁾
Psychiatric disorders			Anxiety ⁽²⁾	
Cardiac disorders		Tachycardia		Kounis syndrome ⁽¹⁾
Vascular disorders	Flushing, hypertension	Hypotension	Phlebitis, syncope ⁽²⁾ , presyncope ⁽²⁾	
Respiratory, thoracic and mediastinal disorders		Dyspnoea	Bronchospasm ⁽²⁾	
Gastrointestinal disorders	Nausea	Vomiting, dyspepsia, abdominal pain, constipation, diarrhoea	Flatulence	
Skin and subcutaneous tissue disorders		Pruritus, urticaria, erythema, rash ⁽³⁾	Angioedema ⁽²⁾ , pallor ⁽²⁾ , distant skin discolouration ⁽²⁾	Face oedema ⁽¹⁾
Musculoskeletal and connective tissue disorders		Myalgia, back pain, arthralgia, pain in extremity, muscle spasms		Hypophosphataemic osteomalacia ⁽¹⁾
General disorders and administration site conditions	Injection/infusion site reactions ⁽⁴⁾	Pyrexia, fatigue, chest pain, oedema peripheral, chills	Malaise, influenza like illness (whose onset may vary from a few hours to several days) ⁽²⁾	
Investigations		Alanine aminotransferase increased, aspartate aminotransferase increased, gamma-glutamyltransferase increased, blood lactate dehydrogenase increased, blood alkaline phosphatase increased		

1 ADRs exclusively reported in the post-marketing setting; estimated as rare.

2 ADRs reported in the post-marketing setting which are also observed in the clinical setting.

- 3 Includes the following preferred terms: rash (individual ADR determined to be uncommon) and rash erythematous, -generalised, -macular, -maculo-papular, -pruritic (all individual ADRs determined to be rare).
- 4 Includes, but is not limited to, the following preferred terms: injection/infusion site -pain, -haematoma, -discolouration, -extravasation, -irritation, -reaction, (all individual ADRs determined to be uncommon) and -paraesthesia (individual ADR determined to be rare).

Note: ADR = Adverse drug reaction.

To reports any side effect(s):

Saudi Arabia:

The National Pharmacovigilance Centre (NPC):

SFDA Call Center: 19999

E-mail: npc.drug@sfd.gov.sa

Website: <https://ade.sfd.gov.sa/>

4.9 Overdose

Accidentally exceeding the cumulative total dose, which is necessary for correcting iron deficiency, can lead to accumulation of iron in the iron stores and ultimately to haemosiderosis in these patients. This can be prevented by preventive control of the iron parameters serum ferritin and transferrin saturation. An unwanted accumulation of iron is to be treated according to standard medical practice.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Iron trivalent, parenteral preparation, ATC code: B03AC

Ferinject solution for injection/infusion is a colloidal solution of the iron complex ferric carboxymaltose.

The complex is designed to provide, in a controlled way, utilisable iron for the iron transport and storage proteins in the body (transferrin and ferritin, respectively).

Red cell utilisation of ^{59}Fe from radio-labelled Ferinject ranged from 91% to 99% in subjects with iron deficiency (ID) and 61% to 84% in subjects with renal anaemia at 24 days post-dose.

Ferinject treatment results in an increase in reticulocyte count, serum ferritin levels and TSAT levels to within normal ranges.

Clinical efficacy and safety

The efficacy and safety of Ferinject has been studied in different therapeutic areas necessitating intravenous iron to correct iron deficiency. The main studies are described in more detail below.

Cardiology

Chronic heart failure

Study CONFIRM-HF was a double-blind, randomised, 2-arm study comparing Ferinject (n=150) vs. placebo (n=151) in subjects with chronic heart failure and ID for a treatment period of 52 weeks. At Day 1 and Week 6 (correction phase), subjects received either Ferinject according to a simplified dosing grid

using baseline Hb and body weight at screening (see section 4.2), placebo or no dose. At Weeks 12, 24, and 36 (maintenance phase) subjects received Ferinject (500 mg iron) or placebo if serum ferritin was <100 ng/mL or 100-300 ng/mL with TSAT <20%. The treatment benefit of Ferinject vs. placebo was demonstrated with the primary efficacy endpoint, the change in the 6-minute walk test (6MWT) from baseline to Week 24 (33 ± 11 , $p=0.002$). This effect was sustained throughout the study to Week 52 (36 ± 11 metres, $p<0.001$).

Study EFFECT-HF was an open-label (with blinded endpoint evaluation), randomised, 2-arm study comparing Ferinject (n=86) vs. standard of care (n=86) in subjects with chronic heart failure and ID for a treatment period of 24 weeks. At Day 1 and Week 6 (correction phase), subjects received either Ferinject according to a simplified dosing grid using baseline Hb and body weight at screening (see section 4.2) or standard of care. At Week 12, (maintenance phase) subjects received Ferinject (500 mg iron) or standard of care if serum ferritin <100 ng/ml or 100 to 300 ng/ml and TSAT <20%. The treatment benefit of Ferinject vs. standard of care was demonstrated with the primary efficacy endpoint, the change in weight-adjusted peak VO₂ from baseline to Week 24 (LS Mean 1.04 ± 0.44 , $p=0.02$).

Nephrology

Haemodialysis-dependent chronic kidney disease

Study VIT-IV-CL-015 was an open-label, randomised parallel group study comparing Ferinject (n=97) to iron sucrose (n=86) in subjects with ID anaemia undergoing haemodialysis. Subjects received Ferinject or iron sucrose 2-3 times per week in single doses of 200 mg iron directly into the dialyser until the individually calculated cumulative iron dose was reached (mean cumulative dose of iron as Ferinject: 1,700 mg). The primary efficacy endpoint was the percentage of subjects reaching an increase in Hb of ≥ 1.0 g/dL at 4 weeks after baseline. At 4 weeks after baseline, 44.1% responded to treatment with Ferinject (i.e. Hb increase of ≥ 1.0 g/dL) compared to 35.3% for iron sucrose ($p=0.2254$).

Non-dialysis-dependent chronic kidney disease

Study 1VIT04004 was an open-label, randomised active-control study, evaluating the safety and efficacy of Ferinject (n=147) vs. oral iron (n=103). Subjects in the Ferinject group received 1,000 mg of iron at baseline and 500 mg of iron at days 14 and 28, if TSAT was <30% and serum ferritin was <500 ng/mL at the respective visit. Subjects in the oral iron arm received 65 mg iron TID as ferrous sulphate from baseline to day 56. Subjects were followed-up until day 56. The primary efficacy endpoint was the percentage of subjects achieving an increase in Hb of ≥ 1.0 g/dL anytime between baseline and end of study or time of intervention. This was achieved by 60.54% of subjects receiving Ferinject vs. 34.7% of subjects in the oral iron group ($p<0.001$). Mean haemoglobin change to day 56/end of study was 1.0 g/dL in the Ferinject group and 0.7 g/dL in the oral iron group ($p=0.034$, 95% CI: 0.0, 0.7).

Gastroenterology

Inflammatory bowel disease

Study VIT-IV-CL-008 was a randomised, open-label study which compared the efficacy of Ferinject vs. oral ferrous sulphate in reducing ID anaemia in subjects with inflammatory bowel disease (IBD). Subjects received either Ferinject (n=111) in single doses of up to 1,000 mg iron once per week until the individually calculated iron dose (per Ganzoni formula) was reached (mean cumulative iron dose: 1,490 mg), or 100 mg iron BID as ferrous sulphate (n=49) for 12 weeks. Subjects receiving Ferinject showed a mean increase in Hb from baseline to Week 12 of 3.83 g/dL, which was non-inferior to 12 weeks of twice daily therapy with ferrous sulphate (3.75 g/dL, $p=0.8016$).

Study FER-IBD-07-COR was a randomised, open-label study comparing the efficacy of Ferinject vs. iron sucrose in subjects with remitting or mild IBD. Subjects receiving Ferinject were dosed according to a simplified dosing grid using baseline Hb and body weight (see section 4.2) in single doses up to 1,000 mg iron, whereas subjects receiving iron sucrose were dosed according to individually calculated iron doses using the Ganzoni formula in doses of 200 mg iron until the cumulative iron dose was reached. Subjects were followed-up for 12 weeks. 65.8% of subjects receiving Ferinject (n=240; mean cumulative iron dose: 1,414 mg) vs. 53.6% receiving iron sucrose (n=235; mean cumulative dose 1,207 mg; p=0.004) had responded at Week 12 (defined as Hb increase ≥ 2 g/dL). 83.8% of Ferinject-treated subjects vs. 75.9% of iron sucrose-treated subjects achieved a Hb increase ≥ 2 g/dL or had Hb within normal limits at Week 12 (p=0.019).

Women's health

Post partum

Study VIT-IV-CL-009 was a randomised open-label non-inferiority study comparing the efficacy of Ferinject (n=227) vs. ferrous sulphate (n=117) in women suffering from post-partum anaemia. Subjects received either Ferinject in single doses of up to 1,000 mg iron until their individually calculated cumulative iron dose (per Ganzoni formula) was reached, or 100 mg of iron as oral ferrous sulphate BID for 12 weeks. Subjects were followed-up for 12 weeks. The mean change in Hb from baseline to Week 12 was 3.37 g/dL in the Ferinject group (n=179; mean cumulative iron dose: 1,347 mg) vs. 3.29 g/dL in the ferrous sulphate group (n=89), showing non-inferiority between the treatments.

Pregnancy

Intravenous iron medicines should not be used during pregnancy unless clearly necessary. Treatment with Ferinject should be confined to the second and third trimester if the benefit is judged to outweigh the potential risk for both the mother and the foetus, see section 4.6.

Limited safety data in pregnant women are available from study FER-ASAP-2009-01, a randomised, open-label, study comparing Ferinject (n=121 vs oral ferrous sulphate (n=115) in pregnant women in the second and third trimester with ID anaemia for a treatment period of 12 weeks. Subjects received Ferinject in cumulative doses of 1,000 mg or 1,500 mg of iron (mean cumulative dose: 1,029 mg iron) based on Hb and body weight at screening, or 100 mg of oral iron BID for 12 weeks. The incidence of treatment related adverse events was similar between Ferinject treated women and those treated with oral iron (11.4% Ferinject group; 15.3% oral iron group). The most commonly reported treatment-related adverse events were nausea, upper abdominal pain and headache. Newborn Apgar scores as well as newborn iron parameters were similar between treatment groups.

Ferritin monitoring after replacement therapy

There is limited data from study VIT-IV-CL-008 which demonstrates that ferritin levels decrease rapidly 2-4 weeks following replacement and more slowly thereafter. The mean ferritin levels did not drop to levels where retreatment might be considered during the 12 weeks of study follow up. Thus, the available data does not clearly indicate an optimal time for ferritin retesting although assessing ferritin levels earlier than 4 weeks after replacement therapy appears premature. Thus, it is recommended that further re-assessment of ferritin should be made by the clinician based on the individual patient's condition.

5.2 Pharmacokinetic properties

Absorption

Not applicable.

Distribution

After a single Ferinject dose of 100 to 1000 mg iron in patients with iron deficiency, peak total serum iron levels of 37 µg/ml to 333 µg/ml were measured after 15 minutes and 1.21 hours, respectively. The volume of distribution of the central compartment corresponds to the plasma volume (approximately 3 litres).

It was shown by means of positron emission tomography (PET) that iron from radiolabelled Ferinject was eliminated from the blood and transported into the bone marrow and into the reticuloendothelial system of the liver and spleen.

Metabolism

Ferric carboxymaltose is mainly taken up in the reticuloendothelial system of the liver, bone marrow and to a small extent in the spleen, and is then broken down into the components iron hydroxide and carbohydrates, with the iron being bound as ferritin. The iron is made available for erythropoiesis via transferrin, as required. The carbohydrate breakdown products are maltotetraose, maltotriose, maltose and glucose.

Elimination

The plasma clearance of the administered iron was rapid with a terminal half-life of 7 to 12 hours and a mean residence time (MRT) of 11 to 18 hours. The renal elimination of iron was negligible.

Kinetics in specific patient groups

No studies with children have been conducted.

No studies in liver insufficiency have been performed.

5.3 Preclinical data

Pre-clinical data revealed no special hazard for humans based on conventional studies of safety pharmacology, repeat dose toxicity and genotoxicity. Pre-clinical studies indicate that iron released from Ferinject crosses the placental barrier and is excreted in milk in limited, controlled amounts. In reproductive toxicology studies using iron replete rabbits Ferinject was associated with minor skeletal abnormalities in the fetus at maternally toxic levels. In a fertility study in rats, there were no effects on fertility for either male or female animals. These effects are considered transient, as no findings could be observed in the pre/postnatal development.

The highest non-lethal intravenously administered single dose in rodents was 1000 mg iron/kg body weight. No long-term studies in animals have been performed to evaluate the carcinogenic potential of Ferinject. No evidence of allergic or immunotoxic potential has been observed. A controlled in-vivo test demonstrated no cross-reactivity of Ferinject with anti-dextran antibodies. No local irritation or intolerance was observed after intravenous administration.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium hydroxide (for pH adjustment)

Hydrochloric acid (for pH adjustment)

Water for injections

6.2 Incompatibilities

Ferinject may only be mixed with sterile 0.9% w/v saline solution. There are no compatibility studies with containers made of materials other than polyethylene or glass.

6.3 Shelf life

Shelf-life of the product as packaged for sale:

3 years.

Shelf life after opening of the vial:

Use the product immediately for microbiological reasons.

Shelf life after dilution with sterile 0.9% saline solution:

Use the solution for infusion (after dilution) as soon as possible for microbiological reasons. It has been shown that the diluted Ferinject solution is chemically stable at room temperature for 12 hours..

Ferinject may only be used up to the date on the packaging marked “EXP”.

6.4. Special precautions for storage

Prescribed storage conditions: Store in the original packaging and not above 30°C. Do not freeze.

6.5. Nature and contents of container

Ferinject is supplied in a vial (type I glass) with a stopper (bromobutyl rubber) and an aluminium cap as: 10 mL solution containing 500 mg iron. Available in pack sizes of 1 and 5 vials.

6.6 Special precautions for disposal and other handling

The vials are intended for single use only.

Prior to use, the vials should be inspected for visible particles and damage. Only solutions that are homogenous and free of visible particles should be used.

Ferinject must only be mixed with 0.9% w/v sodium chloride solution. Other intravenous diluting solutions and medicinal products must not be used because there is a risk of sediment formation and/or interaction. For instructions on dilution, see section “Posology and method of administration”.

7. MARKETING AUTHORISATION HOLDER

Vifor (International) Inc.
Rechenstrasse 37
9014 St. Gallen
Switzerland

Manufactured by IDT Biologika GmbH, Germany and SPIMACO, Al-Qassim Pharmaceutical Plant Saudi Arabia for Vifor (International) Inc.

8. MARKETING AUTHORIZATION NUMBER

1x10ml vials: 2-557-15
5x10ml vials: 1-557-15

9. DATE OF FIRST AUTHORIZATION / RENEAL OF THE AUTHORIZATION

Date of the first authorization: 03 August 2015
Date of the last renewal: 10 December 2020

10. DATE OF REVISION TEXT

Jan 2023