FERROSPEY

Instructions for the medicinal product

Composition:
Each 5 ml contains:
Ferric Hydroxide in complex with sucrose eq. to elemental Iron 100 mg
Water for injection USP q.s.

Product Description
Physical properties: Dark Brown Color sterile solution filled in 5 ml amber color glass snap off Ampules.
Chemical name: Ferric Hydroxide in complex with Sucrose (iron Sucrose).
Molecular weight: Between 34,000 - 60,000 Da.
Empirical / Structural formula: [Na2Fe5O8(OH) 3(H2O)]n m(C12H22O11)

ATC Code: B03AC02.

Pharmacodynamics:
Iron sucrose injection is a complex of polynuclear iron (III)-hydroxide in sucrose. It is approved for use in replenishing iron in patients receiving erythropoietin (a hormone that stimulates red blood cell production) and undergoing chronic hemodialysis, which involves filtering the blood in order to remove waste products. In these patients, an iron deficiency is caused by blood loss during the dialysis procedure, increased erythropoiesis (red blood cell production), and insufficient absorption of iron from the gastrointestinal tract.
Iron is essential for the synthesis of hemoglobin, which is responsible for the transport of oxygen throughout the body.
Pharmacokinetics:
After intravenous injection of a single dose containing 100 mg iron, maximum iron levels, averaging 538 µmol/l, in 10 minutes after injection. The volume of distribution of the central compartment correspondes well to the volume of plasma (approximately 3 litres).
The iron rapidly cleares from the plasma, the terminal half-life being approx. 6 h. The volume of distribution at steady state 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 reduces to the pre-dose iron level and about 75% of the dosage of sucrose was excreted.

Indication:
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.

Recommended Dose and Mode of Administration
Must be administered only by the 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, should be given a test dose of Ferrospey. Must not be used for intramuscular injection. If during the period of observation emerged the phenomenon of intolerance, the introduction of the drug should be discontinued immediately. Before opening the ampoule, first should inspect it for any possible sediment and damage.
Intravenous drip infusion:
The drug is preferably added during drip infusion in order to reduce the risk of significant decrease of blood pressure and the risk of solution into paravenous space. Immediately before infusion the drug must be diluted only in sterile 0.9% sodium chloride solution in a ratio of 1:20 - e.g. 1 ml (20 mg Fe) in 20 ml 0.9% sodium chloride solution. Dilution must take place immediately prior to infusion and the solution should be administered as follows: 100 mg iron (5 ml Ferrospey) in at least 15 minutes, 200 mg iron (10 ml Ferrospey) in at least 30 minutes, 300 mg (15 ml Ferrospey) - in at least 1.5 hours, 400 mg - in at least 2.5 hours, 500 mg - in at least 3.5 hours. Introduction of maximum tolerated single dose is 7 mg Fe / kg, must be carried out in at least 3.5 hours, regardless of the total dose.
The first 20 mg of iron (i.e. 1 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 100 mg in 15 minutes.
Intravenous injection: also may be administered by slow intravenous injection at a rate of 1 ml undiluted solution per minute and not exceeding 10 ml the drug (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. After injection, to patient is recommended to fix the arm in an extended position.
Injection into dialyser: 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.
Adult Patients with Hemodialysis Dependent-Chronic Kidney Disease:
100 mg undiluted as a slow intravenous injection over 2 to 5 minutes, or as an infusion of 100 mg diluted in a maximum of 100 mL of 0.9% NaCl over a period of at least 15 minutes, per consecutive hemodialysis session. Ferrospey should be administered early during the dialysis session.
The usual total treatment course of Ferrospey is 1000 mg. Ferrospey treatment may be repeated if iron deficiency reoccurs.
Adult Patients with Non-Dialysis Dependent-Chronic Kidney Disease:
200 mg undiluted as a slow intravenous injection over 2 to 5 minutes or as an infusion of 200 mg in a maximum of 100 ml of 0.9% NaCl over a period of 15 minutes. Administer on 5 different occasions over a 14 day period. There is limited experience with administration of an infusion of 500 mg of Ferrospey, diluted in a maximum of 250 ml of 0.9% NaCl, over a period of 3.5 to 4 hours on day 1 and day 14. Ferrospey treatment may be repeated if iron deficiency reoccurs.
Adult Patients with Peritoneal Dialysis Dependent-Chronic Kidney Disease:
In 3 divided doses, given by slow intravenous infusion, within a 28 day period: 2 infusions each of 300 mg over 1.5 hours 14 days apart followed by one 400 mg infusion over 2.5 hours 14 days later. Dilute Ferrospey in a maximum of 250 ml of 0.9% NaCl. Ferrospey treatment may be repeated if iron deficiency reoccurs.
Pediatric Patients (2 years of age and older) with HDD-CKD for iron maintenance treatment:
The dosing for iron replacement treatment in pediatric patients with HDD-CKD has not been established.
For iron maintenance treatment: Administer Ferrospey at a dose of 0.5 mg/kg, not to exceed 100 mg per dose, every two weeks for 12 weeks given undiluted by slow intravenous injection over 5 minutes or diluted in 25 ml of 0.9% NaCl and administered over 5 to 60 minutes. Ferrospey treatment may be repeated if necessary.

Pediatric Patients (2 years of age and older) with NDD-CKD or PDD-CKD who are on erythropoietin therapy for iron maintenance treatment:
The dosing for iron replacement treatment in pediatric patients with NDD-CKD or PDD-CKD has not been established.
For iron maintenance treatment: Administer Ferrospey at a dose of 0.5 mg/kg, not to exceed 100 mg per dose, every four weeks for 12 weeks given undiluted by slow intravenous injection over 5 minutes or diluted in 25 ml of 0.9% NaCl and administered over 5 to 60 minutes. Ferrospey treatment may be repeated if necessary.

Contraindications:
- Known hypersensitivity to the drug or any of its excipients;
- Anaemias not attributable to iron deficiency;
- Iron overload or disturbances in utilisation of iron;
- Pregnancy first trimester.

Warnings and Precautions
Asthma, eczema, polyvalent allergy, allergic reactions to other parenteral iron preparations, liver failure, acute infectious diseases, low serum iron binding capacity and / or folic acid deficiency, diabetes, children's age (under 18) (due to the insufficient data on safety and efficacy).
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 Ferrospey at the injection site may lead to pain, inflammation, tissue necrosis and brown discoloration of the skin.

Interactions with Other medicaments:
As with all parenteral iron preparations, Ferrospey should not be administered concomitantly with oral iron preparations since the absorption of oral iron is reduced. Therefore, oral iron therapy should be started at least 5 days after the last injection.
Ferrospey must only be mixed with sterile 0.9% m/V sodium chloride solution. No other solutions and therapeutic agents should be used as there is the potential for precipitation and/or interaction.
The compatibility with containers other than glass, polyethylene and PVC is not known.
If the patients is taking other medications, they should consult with doctor.

Pregnancy and Lactation
Contraindicated in I trimester of pregnancy. May use in II and III trimester of pregnancy only if the expected benefit to the mother outweighs the potential risk to the fetus. During lactation the safety of the drug has not been established. It is recommended to stop breast-feeding (if necessary, use) or stop medication.

Undesirable Effects:
CNS: transient taste perversions (in particular metallic taste), headache, dizziness, paraesthesia, syncope, loss of consciousness, burning sensation.
Cardio-vascular system: hypotension and collapse, tachycardia, palpitations, and hypertension.
Respiratory system: bronchospasm, dyspnoea.
Gastrointestinal disorders: nausea; vomiting, abdominal pain, diarrhoea.
Skin and subcutaneous tissue disorders: pruritus, urticaria, rash, exanthema, erythema.
Musculoskeletal, connective tissue and bone disorders: muscle cramps, myalgia.
General disorders and administration site disorders: fever, shivering, flushing, chest pain and tightness. Injection site disorders such as superficial phlebitis, burning, swelling. Rare - arthralgia, peripheral oedema, fatigue, asthenia, malaise, feeling hot, oedema.
Immune system disorders: rare - anaphylactoid reactions.
Isolated cases: reduced level of consciousness, light-headed feeling, confusion, angio-oedema, swelling of joints, hyperhidrosis, back pain, bradycardia, chromaturia.
Injection site discoloration following extravasation. Ensure stable intravenous access to avoid extravasation.

Overdose and Treatment:
Symptoms: decreased blood pressure (signs of collapse are evident within 30 minutes), hemosiderosis symptoms.
Treatment: symptomatic, if necessary - drugs that bind iron (chelating), such as deferoxamine.

Dosage Forms and Packaging Available:
1X5, 5 ml ampoule in a plastic tray in a carton box, with instruction for use.

Storage:
Keep in dry place protected from light at a temperature below 30°C. Keep out of reach of children.

Shelf life:
2 years. Do not use after expiry date.

Distribution Condition:
Prescription only medicine (POM).

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