Xenofer®

Iron Sucrose USP Injection

COMPOSITION

Xenofer® Injection : Each ampoule contains 5 ml solution of 20 mg/ml Iron as Iron Sucrose USP corresponding to 100 mg elemental Iron.

PHARMACOLOGICAL INFORMATION

Therapeutic class: Hematinic

Pharmacological Action

Administration of **Xenofer®** replenishes tissue iron stores, reverses iron depletion and iron-deficient erythropoiesis, and corrects or prevents iron deficiency anemia.

Mechanism of Action

Following intravenous administration, **Xenofer®** (Iron Sucrose) is dissociated into iron and sucrose by the reticuloendothelial system and iron is transferred from the blood to a pool of iron in the liver and bone marrow. Ferritin, an iron storage protein, binds and sequesters iron in a nontoxic form, from which iron is easily available. Iron binds to plasma transferrin, which carries iron within the plasma and the extracellular fluid to supply the tissues. The transferrin receptor, located in the cell membrane, binds the transferrin iron complex, which is then internalized in vesicles. Iron is released within the cell, and the transferrin-receptor complex is returned to the cell membrane. Transferrin without iron (apotransferrin) is then released to the plasma. The intracellular iron becomes (mostly) hemoglobin in circulating red blood cells (RBCs). Transferrin synthesis is increased and ferritin production reduced in iron deficiency. The converse is true when iron is plentiful.

PHARMACOKINETIC PROPERTIES

Iron disappearance from serum depends on the need for iron in the iron stores and iron utilizing tissues of the body, serum clearance of iron is expected to be more rapid in iron deficient patients treated with Iron Sucrose as compared to healthy individuals. The effects of age and gender on the pharmacokinetics of Iron Sucrose have not been studied. Distribution: Following intravenous doses of Iron Sucrose, the iron component appears to distribute mainly in blood and to some extent in extra vascular fluid. Following IV administration iron may also distribute to some extents in the liver, spleen and bone marrow. Metabolism and Elimination: The sucrose component is eliminated mainly by urinary excretion.

CLINICAL INFORMATION

Therapeutic Indications : **Xenofer®** (Iron Sucrose) is indicated in the treatment of iron deficiency in the following indications:

- Where there is a clinical need for a rapid iron supply,
- In patients who cannot tolerate oral iron therapy or who are non-compliant,
- In active inflammatory bowel disease where oral preparations are ineffective.

Treatment of iron deficiency anemia in Pregnancy and in non-dialysis dependent chronic kidney disease (CKD) patients either receiving or not receiving an erythropoietin, hemodialysis dependent-CKD patients receiving an erythropoietin, or peritoneal dialysis-CKD patients receiving an erythropoietin.

Dosage

Calculation of dosage : The dosage has to be individually adapted 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]
Up to 35 kg body weight : target Hb = 130 g/l respectively depot iron =15 mg/kg body weight.
Above 35 kg body weight : target Hb = 150 g/l respectively depot iron = 500 mg
*Factor 0.24 =0.0034 x 0.07 x 1000 (Iron content of Hb = 0.34%/ Blood volume = 7% of body wt / Factor 1000 = conversion from gm to mg)

Total amount of **Xenofer®** to be administered (in ml) $= \frac{\text{Total iron deficit (mg)}}{\text{20 mg/ml}}$

Calculation of No. of Ampoules required for different body weight and different hemoglobin level

Hb Level	5 kg	10 kg	15 kg	20 kg	25 kg	30 kg	35 kg	40 kg	45 kg	50 kg	55 kg	60 kg	65 kg	70 kg	75 kg	80 kg	85 kg	90 kg
Hb 60 g/l	1.5	3	5	6.5	8	9.5	12.5	13.5	15	16	17	18	19	20	21	22.5	23.5	24.5
Hb 75 g/l	1.5	3	4.5	5.5	7	8.5	11.5	12	13	14	15	16	16.5	17.5	18.5	19.5	20.5	21.5
Hb 90 g/l	1.5	2.5	3.5	5	6	7.5	10	11	11.5	12	13	13.5	14.5	15	16	16.5	17	18
Hb 105 g/l	1	2	3	4	5.5	6.5	9	9.5	10	10.5	11	11.5	12	12.5	13	13.5	14	14.5

Calculation of dosage for iron replacement secondary to blood loss and to support autologous blood donation : The required **Xenofer®** dose to compensate the iron deficit is calculated according the following formulas:
- if the quantity of blood lost is known: The administration of 200 mg IV iron (=10 ml **Xenofer®**) results in an increase in Hb which is equivalent to 1 unit blood.
Iron to be replaced [mg] = number of blood units lost x 200 or
Amount of **Xenofer®** needed (ml) = number of blood units lost x 10
- If the Hb level is reduced: use the previous formula considering that the depot iron does not need to be restorted.
Iron to be replaced [mg] = body weight [kg] x 0.24 x (target Hb - actual Hb) [g/l]

Adults and the Elderly : **Xenofer®** has exclusively to be administered intravenously by slow injection or by drip infusion or directly into the venous limb of the dialyser. **Xenofer®** must not be used for intramuscular injection.
As infusion : **Xenofer®** should preferably be administered by drip infusion (in order to reduce hypotensive episodes) in a dilution of 1 ml **Xenofer®** in max. 20 ml 0.9% NaCl etc up to 25 ml **Xenofer®** in max. 500 ml 0.9% NaCl. Dilution must take place immediately prior to infusion and solution must be administered as follows : 100 mg Iron in at least 15 minutes; 200 mg Iron in at least 30 minutes etc. Normal posology is to use 5-10 ml **Xenofer®** once to three times a week depending on the hemoglobin level. For the administration of the maximum tolerated dose of 7 mg Iron/kg body weight an infusion time of at least 3.5 hours has to be respected, independently of the total dose.
As injection : **Xenofer®** can also be administered undiluted by slow IV injection at a rate of 1 ml **Xenofer®** (20 mg iron) in at least 1 min. A maximum of 10 ml **Xenofer®** (200 mg iron) can be administered per injection in at least 10 minutes.

Children : If there is a clinical need, it is recommended not to exceed 0.15 ml **Xenofer®** (3 mg iron) per kg body weight once to three times a week as IV infusion depending on the hemoglobin level.

Administration

Mode	Direct into IV tubing	Intermittent Infusion
Adult	Undiluted, doses of 100-200 mg over 5-10 minutes. Doses greater than 200 mg should be administered by intermittent infusion.	Dilute 100 mg in 50-100 ml Normal Saline. (Infuse over 15-30 minutes). Dilute 200 mg in 100-200 ml Normal Saline. (Infuse over 30-60 minutes).
Pediatric	No information	Dilute 25 mg in 25 ml Normal Saline. Dilute 50 mg in 50 ml Normal Saline. (Infuse over 15-30 minutes).
Neonate	No information	For doses 100 mg or greater as above. Dilute to 0.5-2 mg/ml with Normal Saline. (Infuse over 2-6 hours).
Requirements	IV infusion device for intermittent infusion. Test dose not required.	

If any allergic reactions or intolerance occurs during administration, the therapy must be stopped immediately.

Use in pregnancy & lactation
Pregnant women : FDA pregnancy category B.

Undesirable effects
Occasionally metallic taste, headache, nausea, vomiting and hypotension can occur. Less frequently parasthesia, abdominal disorders, muscular pain, fever, urticaria, flushing, edema of the extremities, anaphylactoid (pseudoallergic) reactions and in the region of the punctured vein, phlebitis and venous spasm have been observed.

Contraindications
The use of Iron Sucrose is contraindicated in patients with evidence of iron overload, in patients with known hypersensitivity to Iron preparations or any of its inactive components, in patients with anemia not caused by iron deficiency and in the first trimester of pregnancy.

Precaution
Iron Sucrose should be administered with caution in patients with asthma, eczema, other atopic allergies or allergic reaction to other parenteral iron preparations, low binding capacity and/or folic acid deficiency, liver dysfunction, acute or chronic infection.
Baseline tests : Ensure Hgb, Hct, serum ferritin, and transferrin saturation are determined before starting therapy and periodically during treatment. Note that serum iron levels may be reliably obtained 48 hours after IV dosing.
BP : Monitor BP during infusion. If hypotension occurs, slow infusion rate. If hypotension continues, discontinue infusion and be prepared to treat appropriately.

- Discontinue oral iron preparations before administering parenteral iron products. Co-administration of parenteral iron preparations may reduce absorption of oral iron.
- The dosage is expressed in terms of elemental iron.
- For IV administration only. Not for intradermal, subcutaneous, IM or intra-arterial administration.
- Medication is administered 1 to 3 times/ week. Do not administer more than 3 times/ week.
- For IV infusion in adults, dilute contents of 1 apmoule in 100 ml sodium chloride 0.9% injection immediately prior to infusion and infuse over 15 min.
- Discard any unused diluted solution. Do not save unused solution for future use.
- Do not administer if particulate matter or discoloration noted.
- Concomitant administration of oral and parenteral iron may lead to complications from iron overload.

Drug Interactions
Iron Sucrose should not be administered concomitantly with oral iron preparations since the absorption of oral iron is reduced.
Incompatibility : Do not mix with other medication or add to parenteral nutrition solutions for IV infusion.

Overdosage
Xenofer® should not be given to people with iron overload and should be stopped when serum ferritin levels equal or exceed established guidelines. Particular caution should be used to avoid iron overload where anemia that does not respond to treatment has been incorrectly diagnosed as iron deficiency anemia. Symptoms associated with overdose or infusing **Xenofer®** too rapidly included hypotension, headache, vomiting, nausea, dizziness, joint aches, paresthesia (abnormal sensation, such as tingling or burning), abdominal and muscle pain, edema, and cardiovascular collapse. Most symptoms have been successfully treated with IV fluids, hydrocortisone, and/or antihistamines. Infusing the solution as recommended or at a slower rate also may alleviate symptoms.

PHARMACEUTICAL INFORMATION
Storage Conditions
Store in original carton. Do not store above 25°C. Do not freeze. Keep out of the reach of children. Use immediately after dilution in saline.

Presentation & Packaging
Xenofer® Injection (1 X 1's): Each commercial box contains 1 amber ampoule containing 5 ml Iron Sucrose injection in drawer box, 1 bottle of Xenosol 100 IV infusion, 1 disposable syringe (5 ml), 1 infusion set with butterfly needle, 1 plastic hanger, first aid band & alcohol pad.

Manufactured By
BEACON®
Pharmaceuticals PLC
Bhaluka, Mymensingh, Bangladesh

LF03405