SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

1.1 Brand Name **:** AKUROSE

1.2 Generic Name **:** IRON SUCROSE INJECTION USP

1.3 Strength **:** 20mg/ml

1.4 Pharmaceutical Form: Injection

2. QUALITY AND QUANTITATIVE COMPOSITION

Each ml contains:

Iron Sucrose Eq to Elemental Iron 20 mg
Water for Injection USP ……q.s.

3. PHARMACEUTICAL FORM VISUAL DESCRIPTION:

Dark brown colour solution filled in amber coloured glass ampoule.

4. CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS:

Akurose 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 in effective.

4.2 POSOLOGY AND METHOD OF ADMINISTRATION

Administrations: Akurose must only be administered by the intravenous route. This may be by a slow intravenous injection or by an intravenous drip infusion.

Akurose must not be used for intramuscular injections.

Adults & the elderly: The total cumulative dose of Akurose, equivalent to the total iron deficit (mg), is determined by the haemoglobin level and body weight. The dose for Akurose 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) * (Target Hb – Actual Hb) [g/l]* 0.24 + Depot iron (mg)

Dosage: The total single dose must not exceed 200mg 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: The use of Akurose has not been adequately studied in children &, therefore, Akurose is not recommended for use in children.

Intravenous drip infusion: Akurose must be diluted only in sterile 0.9% m/V sodium chloride solution:

- 2.5ml Akurose (50mg iron)
  In max. 50ml sterile 0.9% m/V sodium chloride solution
- 5ml Akurose (100mg iron)
  In max. 100ml sterile 0.9% m/V sodium chloride solution
- 10ml Akurose (200mg iron)
  In max. 200ml sterile 0.9 % m/V sodium chloride solution

For Stability reasons, dilutions to lower Akurose concentrations are not permissible.

Dilution must take place immediately prior to infusion & the solution should be administered as follows:

- 100mg iron (5ml Akurose) in at least 15 minutes
- 200mg iron (10ml Akurose) in at least 30 minutes

Intravenous Injection: Akurose may be administered by slow intravenous injection at a rate of 1ml undiluted solution per minute and not exceeding 10ml Akurose (200mg iron) per injection.

Injection into dialyser: Akurose 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.

4.3 CONTRAINDICATIONS

The use of Akurose is contraindicated in cases of:

- Hypersensitivity to the active substance
- Known Serious hypersensitivity to other parenteral iron products
- Anaemias not attributable to iron deficiency
- Iron overload or disturbances in utilisation of iron

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Parenterally administered iron preparations can cause hypersensitivity reactions including serious and Potentially fatal anaphylactic/anaphylactoid reactions. Hypersensitivity reactions have also been reported after previously uneventful doses of parenteral iron complexes.

The risk is enhanced for patients with known allergies including drug allergies, including patient with a history of severe asthma, eczema or other atopic allergy.

There is also an increased risk of hypersensitivity reactions to parenteral iron complexes in patient with immune or inflammatory conditions (e.g. systemic lupus erythematosus, rheumatoid arthritis).

Akurose 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. Each patient should be observed for adverse effect for atleast 30 minutes following each Akurose injection. If hypersensitivity reactions or signs of intolerance occur during administration, the treatment must be stopped immediately. Facilities for cardio respiratory resuscitation and equipment for handling acute anaphylactic/anaphylactoid reactions should be available, including an injectable 1: 1000

adrenaline solution. Additional treatment with antihistamines and/or corticosteroids should be given as appropriate.

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 patient 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 Akurose at the injection site may lead to pain, inflammation, tissue necrosis and brown discoloration of the skin.

4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTIONS

As with all parenteral iron preparations, Akurose 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 of Akurose.

4.6 PREGNANCY AND LACTATION

Pregnancy

There are no adequate and well controlled trials of Akurose in pregnant women. A careful risk/benefit evaluation is therefore required before use during pregnancy & Akurose should not be used during pregnancy unless clearly necessary.

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

Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development. Data on a limited number of exposed human pregnancies indicated no adverse effects of Akurose on pregnancy or on the health of the foetus/newborn child.

Breastfeeding

Non metabolised Akurose is unlikely to pass into the mother milk. No well controlled clinical studies are available to date. Animal studies do not indicate direct or indirect harmful effects to the nursing child.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINE

In case of symptoms of dizziness, confusion or light headedness following the administration of Akurose, Patient should not drive or use machinery until symptoms have ceased.

4.8 UNDESIRABLE EFFECTS

Transient taste perversions (in particular metallic taste), Hypotension, Tachycardia, Palpitations, Bronchospasm, Dyspnoea, Nausea; Vomiting, Abdominal Pain, Diarrhoea, Pruritus, Urticaria, Rash, Exanthema, Erythema, Muscle Cramps, Myalgia, fever, Shivering, Flushing, Chest Pain, Tightness, Burning Swelling.

4.9 OVERDOSE:

Overdosage can cause acute iron overloading which may manifest itself as haemosiderosis. Overdosage should be treated, if required, with an iron chelating agent.

5. PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMICS PROPERTIES

Iron Sucrose is a dark brown, slightly viscous sterile liquid complex of ferric hydroxide and sucrose for intravenous or intramuscular use. After iron sucrose is injected, the circulating iron sucrose is removed from the plasma by cells of the reticuloendothelial system, which splits the complex into its components of iron and sucrose. The iron is immediately bound to the available protein moieties to form hemosiderin or ferritin, the physiological forms of iron, or to a lesser extent to transferrin. This iron which is subject to physiological control replenishes haemoglobin and depleted iron stores.

5.2 PHARMACOKINETIC PROPERTIES

Following intravenous injection of a single dose of Akurose containing 100mg iron in healthy volunteers, maximum iron level, averaging 538µmol/l, were obtained 10 minutes after injection. The volume of distribution of the central compartment corresponded well to the volume of plasma.

The iron injected was rapidly cleared from the plasma, the terminal half-life being approx. 6h. The volume of distribution at steady state was about 8 litres, indicating a low iron distribution in the body fluid. Due to 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. 31mg 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 level of iron were reduced to the pre-dose iron level and about 75% of the dosage of sucrose was excreted.

5.3 PRECLINICAL SAFETY DATA

None Stated

6. PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Sodium Hydroxide (Pellets) USNF

Water for Injection USP

6.2 INCOMPATIBILITIES

Not applicable

6.3 SHELF LIFE

36 Months

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 30°C, in a dry & dark place. Do not freeze.

6.5 NATURE AND CONTENTS OF CONTAINER

Tray of 5 X 5 ml Ampoule packed in Mono Carton along with insert.

6.6 SPECIAL PRECAUTION FOR DISPOSAL

Not Applicable

7. MARKETING AUTHORIZATION HOLDER

Name	:	UNOSOURCE PHARMA LIMITED
Address	:	503-504, 5th Floor, Hubtown Solaris, N.S. Phadke Marg, Andheri (east), Mumbai – 400 069, INDIA
Phone	:	+91-22-61056105
Fax	:	+91-22-61056106

8. MARKETING AUTHORIZATION NUMBERS

New Registration

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION

Not applicable.

10. DATE OF REVISION OF THE TEXT

Not applicable

11. NAME AND ADDRESS OF THE MANUFACTURER

Name	:	AKUMS DRUGS & PHARMACEUTICALS LTD.
Address	:	Plot No. 2, 3, 4 and 5, sector–6 , IIE, SIDCUL, Ranipur, Haridwar- 249403, Uttarakhand, India.
Phone	:	91-0133-4237100
Fax	:	91-0133-4237105
E-mail	:	inj@akums.in