Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Intralipid 10% Emulsion for Infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Contains soya-bean oil, refined (Purified soybean oil)
10% w/v (100g/l).

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Emulsion for infusion.
Sterile, milky-white, oil-in-water emulsion.
Osmolality: 300 mosm/kg water. pH approximately 8.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For the supply of caloric and essential fatty acids requirements in parenteral nutrition.

4.2 Posology and method of administration

For intravenous infusion.

Posology
The dosage and infusion rate should be within the ranges recommended below and should be governed by the patient's ability to utilise fat.

Recommended dosage for adults: Intralipid 10%: 500-1000 ml per 24 hours in conjunction with amino acid and carbohydrate solutions. For greater energy requirements Intralipid 20% 500-1000 ml per 24 hours may be used instead of Intralipid 10%.

Essential fatty acid deficiency (EFAD):
When Intralipid is administered to prevent or correct essential fatty acid deficiency, 4-8% of non protein calories should be supplied as Intralipid to provide sufficient amounts of linoleic and linolenic acids.

When EFAD is associated with stress, the amount of Intralipid needed to correct the deficiency may be substantially increased.

Recommended dosage for infants:
Dosage is governed by the maturity and birth weight of the infant. In mature infants dosage scheme 1 should be used. In small for gestational age and low birth-weight infants where the ability to handle fat may be impaired, dosage scheme 2 should be utilised.

To all cases, the infant's ability to eliminate infused fat from the circulation should be checked daily. Measuring serum triglycerides is the only reliable method. If lipaemia is present re-testing should be carried out after an interval of four hours.

When administered to infants Intralipid should, if possible, be infused continuously over 24 hours and to maintain a constant rate of infusion it is essential that an appropriate pump is used.

1) Infants: 0.5-4 g fat per kg body weight in 24 hours. In practice 0.02-0.17 g/kg body weight should be administered each hour. The equivalent volumes of Intralipid are 10% 0.21-1.70 ml/kg/hour; 20% 0.10-0.85 ml/kg/hour. The dosage should be gradually increased during the first week of administration.

2) To premature and low birth weight infants, Intralipid should be administered continuously during 24 hours/day. The initial infusion rate should be 0.5 - 1.0 g/kg/24 hours (2.5 - 5.0 ml Intralipid 20%/kg/24 hours). The dose is then increased by the same amount (0.5 - 1.0 g/kg) every 24 hour period up to 2.0 g/kg/24 hours (10 ml Intralipid 20%/kg/24 hours). There should be concomitant careful monitoring of triglyceride levels, liver function tests and oxygen saturation.

The rates given are maximum rates and no attempt should be made to exceed these in order to compensate for missed doses.

Recommended dosage for the elderly: Age per se requires no adjustment of the adult dosage. However, caution should be exercised in the frail elderly and indeed in all patients with poor renal, cardiac or liver function, where smaller volumes should be used depending on the individual's requirements and condition.

Method of administration

Intralipid 10% and 20% are administered by slow intravenous infusion. During the first 10 minutes the drip should be adjusted to 20 drops per minute and then gradually increased to a final rate after half an hour of 25-40 drops per minute for Intralipid 20% and 40-60 drops per minute for Intralipid 10%. 500 ml of Intralipid 20% should be given over a period of not less than five hours.

500 ml of Intralipid 10% should be given over a period not less than three hours. On the first day of infusion it is advisable to administer 5 ml Intralipid 20% per kg body weight or 10 ml Intralipid 10% per kg body weight. Subsequently the dose is usually doubled and when a larger intake is indicated the dosage may be increased to a maximum of 3 g fat per kg body weight per 24 hours.

Intralipid may be given as a separate infusion or as an admixture. When separate infusion is preferred the fat emulsion may be infused into the same central or peripheral vein as carbohydrates/amino acid solutions by means of a Y-connector near the infusion site. Carbohydrates/amino acid infusions are best given into a central vein.

Intralipid can also be given as part of an All in One admixture containing carbohydrates, amino acids, electrolytes, vitamins and trace elements. The admixture must be approved for physical stability.

As with all infusions, care should be taken to avoid complications of catheterisation including air embolism and central venous thrombosis. The risk of serious thoracic complications can be avoided by the use of a peripheral catheter. The provision of intravenous nutrition via a peripheral catheter is facilitated by the near isotonicity of Intralipid. Strict asepsis should be maintained, especially in the immunosuppressed patient.

Monitoring:

Electrolyte, fluid, acid-base imbalance and shock should be corrected prior to commencement of intravenous nutrition. In the metabolic and nutritional management of the seriously ill patient, specific preliminary investigations and continuous monitoring are essential, particularly of electrolyte levels. Monitoring of vitamin and trace element levels should be included, especially in patients receiving long-term intravenous nutrition**.**

4.3 Contraindications

1. Intralipid is contraindicated in severe disorders of fat metabolism such as in severe liver damage and acute shock.
2. Severe liver insufficiency
3. Haemophagocytic syndrome
4. Hypersensitivity of egg, soya or peanut protein or to any of the active substances or excipients.

4.4 Special warnings and precautions for use

Where shock, metabolic acidosis or severe dehydration is presented, the condition should be corrected before commencement of intravenous feeding.

Catheters for IV feeding should be placed using strict aseptic technique with proper fixation and dressing and X-ray confirmation. Asepsis should be maintained during changes of tubing and dressing and use of catheter should be confined to IV feeding alone.

Patients receiving these infusions may suffer from air embolisms, pneumothorax, central venous thrombosis, brachial plexus or thoracic duct injury, catheter-linked sepsis, subdural haematoma (due to anti-coagulants) and infusion thrombophlebitis. Care should be taken to avoid these complications. Immunosuppressed patients are particularly prone to infections.

Abnormalities of liver function tests and cholestasis have been observed in patients including infants receiving total parenteral nutrition. Intralipid may interfere with certain laboratory measurements (bilirubin, lactate dehydrogenase, oxygen saturation, Hb etc) if blood is sampled before fat is adequately cleared from the blood stream. Fat is cleared after a fat free interval of 4 to 6 hours in most patients.

Infusion of 10% fat emulsion has been associated with the development of abnormal lipoprotein, the formation of which is dependent on the dose and duration of the infusion.

Amino-acid and carbohydrate infusion should accompany that if fat emulsion to avoid acidosis.

Intralipid should be given with caution in conditions of lipid metabolism such as renal insufficiency, uncompensated diabetes mellitus, pancreatitis, certain forms of liver insufficiency, hypothyroidism (if hyperglyceridaemic), metabolic disorders and sepsis. Fat embolism has been reported in a few cases when the recommended infusion rate has been exceeded in these patients. Fat elimination should be checked daily if intravenous fat in considered for administration to such patients.

In newborns with neonatal hyperbilrubinaemia, Intralipid should be used with caution, especially in low birth weight infants, because of the risk of free fatty acids displacing bilirubin from albumin.

Intralipid should be administered with caution to infants with known or suspected pulmonary hypertension.

In neonates, particularly premature on long term parenteral nutrition, platelet count, liver test and serum triglyceride concentrates should be monitored.

Patients known to be allergic to soy protein, should not be given to Intralipid.

This medicinal product contains soya-bean oil and egg phospholipids, which may rarely cause allergic reactions. Cross allergic reactions have been observed between soybean and peanut.

Fat Elimination:
The ability to eliminate fat should be closely monitored in patients with conditions mentioned under Precautions and Warnings (this section), but also in patients given Intralipid for more than one week. This is done by collecting a blood sample after a fat-free clearance period of 4-6 hours. Blood cells are then separated from plasma by centrifugation (1200-1500 rotations per minute, rpm). If the plasma is opalescent, the infusion should be postponed. The sensitivity of the method is such that hypertriglyceridaemia can pass undetected. Therefore, it is recommended that serum triglyceride concentrations are measured in patients who are likely to have an impaired fat tolerance.

4.5 Interaction with other medicinal products and other forms of interactions

Some drugs, like insulin, may interfere with body's lipase system. However, this kind of interaction seems to be of only limited clinical importance.

Heparin in clinical doses, causes a transient increase in lipolysis in plasma, resulting in a transient decrease in triglyceride due to depletion of lipoprotein lipase.

Soybean oil has a natural content of vitamin K_1. This is considered important only for patients treated with coumarin derivatives which interfere with Vitamin K_1.

4.6 Fertility, pregnancy and lactation

Animal reproduction studies have not been carried out with Intralipid. There are, however, published reports of its successful and safe administration during pregnancy in humans.

4.7 Effects on ability to drive and use machines

Intralipid 10% has no influence on the ability to drive and use machines.

4.8 Undesirable effects

In rare instances, initial administration of Intralipid has produced a rise in temperature and less frequently, shivering, chills and nausea / vomiting (incidence < 1%). Infusion of Intralipid should be discontinued in such cases.

Other adverse event reports are extremely rare, occurring in less than one in one million infusions.

The following have been reported occurring immediately or soon after commencing infusion: Hypersensitivity reactions (anaphylaxis, skin rash, urticaria), respiratory symptoms (e.g. tachypnoea), circulatory effects (e.g. hyper/hypotension), haemolysis, reticulocytosis, abdominal pain, headache, tiredness and priapism.

Increased levels of transaminases, alkaline phosphatases and bilirubin have been observed in patients receiving intravenous nutrition, with or without Intralipid. If the dosage is reduced values usually return to normal. Cholestasis has also been reported.

Thrombocytopenia has been reported in association with prolonged treatment with Intralipid in infants.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via: HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2.Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; e-mail: medsafety@hpra.ie.

4.9 Overdose

Overdose leading to fat overload syndrome may occur, acutely as a result of too rapid an infusion rate, or chronically at recommended rates of infusion in association with a change in the patients clinical condition, e.g. renal function impairment or infection. Fat overload syndrome is characterised by hyperlipidaemia, fever, fat infiltration, organ dysfunction and coma. All symptoms are usually reversible if the infusion is discontinued.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Intralipid is a concentrated energy source for complete intravenous nutrition. Provision of a sufficient amount of energy in the form of carbohydrate is often restricted by such considerations as hypertonicity, hypervolaemia, tendency to thrombophlebitis and the limit beyond which further carbohydrate cannot be utilised. By the use of Intralipid it is possible to provide a high-energy intake in a relatively small volume.

Intralipid is a rich source of the essential fatty acids, linoleic and linolenic acids. It has a protein sparing effect when given in conjunction with amino acid and carbohydrate solutions.

The pharmacodynamic effects of Intralipid are limited due to the nature of the product. Intralipid is intended to be a substitute for the naturally occurring chylomicrons which enter the blood stream after gastrointestinal absorption of fat.

5.2 Pharmacokinetic properties

Intralipid is metabolised in a similar way to chylomicrons.

5.3 Preclinical safety data

During the preclinical animal studies there were no findings which were of relevance to the prescriber in relation to the safety profile of Intralipid.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium hydroxide (for pH adjustment)
Purified egg phospholipids
Glycerol
Water for injections

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products unless compatability is known.

6.3 Shelf life

2 Years.
Once opened, use immediately and discard any unused contents.

6.4 Special precautions for storage

Do not store above 25°C. Do not freeze.

6.5 Nature and contents of container

The excel bag consist of an inner bag (primary package) with an overpouch.
The inner bag consists of a poly (propylene/ethylene) copolymer, a thermoplastic elastomer and co-polyester.

An oxygen absorber and an integrity indicator (Oxalert^{TM}) are placed between the inner bag and the overpouch. The integrity indicator (Oxalert^{TM}) will react with free oxygen and change colour if the overpouch is damaged.
If the indicator is black, oxygen has penetrated the overpouch and the product should be discarded.

Pack sizes 100ml and 500ml.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

If the indicator is black, oxygen has penetrated the overpouch and the product should be discarded.

Do not use if package is damaged.

After inspection of the integrity indicator, the overpouch, oxygen absorber and integrity indicator should be discarded after opening.

Additions should be made aseptically. Single administration of electrolyte solutions to INTRALIPID should not be made. Additives may only be added to Intralipid where compatibility is known. Such mixing must follow defined formulae and mixing techniques.The following additions can be recommended: Vitlipid N Adult or Vitlipid N Infant, Solivito N (see Solivito N data sheet for details on reconstitution).

For single use only.

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

Do not reconnect partially used bags.

7 MARKETING AUTHORISATION HOLDER

Fresenius Kabi Deutschland GmbH
Else-Kroener Strasse 1

Bad Homburg v.d.H 61352
Germany

8 MARKETING AUTHORISATION NUMBER

PA2059/041/002.

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