SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Intralipid 20%

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient
Purified Soybean Oil Ph. Eur. 20.0% w/v

Product Properties
Intralipid 20%
Energy content 2000 kcal (8.4 mJ)/l
Osmolality 350 mosm/kg water
Organic phosphate content 15 mmol/l*
Triglycerides 20 g/100 ml
pH approx. 8
* This is considered to be bioavailable.

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Lipid emulsion for intravenous infusion.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For use as part of a balanced intravenous feeding regimen in patients who are unable to receive sufficient amounts of nutrients enterally. Intralipid is especially valuable in providing a high energy intake to compensate for increased energy expenditure following trauma, infections, severe burns.

4.2 Posology and method of administration

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 20%: 500-1000 ml per 24 hours in conjunction with intravenous administration of amino acid and carbohydrate solutions. For lesser energy requirements Intralipid 10% 500-1500 ml per 24 hours in conjunction with amino acid and carbohydrate solutions.

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. In 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 over 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). The dose can only be increased above that level and up to a maximum of 4.0 g/kg/24 hours (20 ml Intralipid 20%/kg/24 hours) by concomitant careful monitoring by following the 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. 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 Contra-Indications

Intralipid is contra-indicated in severe disorders of fat metabolism such as in severe liver damage and acute shock.

4.4. Special Warnings and Special Precautions for Use

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

If intravenous administration of fat is considered in patients with the above mentioned disorders, the elimination of fat should be checked daily.

Patients known to be allergic to soy protein, should be given Intralipid with caution and only after hypersensitivity tests.

In new-borns with neonatal hyperbilirubinaemia 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 prematures on long term parenteral nutrition, platelet count, liver test and serum triglyceride concentration should be monitored.

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.

Fat Elimination:
The ability to eliminate fat should be closely monitored in patients with conditions mentioned under Special 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 Interaction

Some drugs, like insulin, may interfere with the 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 20% 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 phosphatase 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 of 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 the Yellow Card Scheme at www.mhra.gov.uk/yellowcard

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 patient's 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

Pharmacotherapeutic group: Solutions for parenteral nutrition, ATC code: B05B A02

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. Pre-clinical 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

Purified egg phospholipids
Glycerol
Sodium hydroxide
Water for Injections

6.2. Incompatibilities

Additives may only be added to Intralipid where compatibility is known. Such mixing must follow defined formulae and mixing techniques, details of which are available on request from the manufacturer. The following additions can be recommended: Vitlipid N Adult or Vitlipid N Infant, Solivito N (See Solivito N data sheet for details on reconstitution).

6.3. Shelf-Life

24 months.

6.4. Special Precautions for Storage

Store below 25°C. Do not freeze.

6.5 Nature and contents of container

All packaging components are latex-free and PVC-free.

Infusion bottle: Type II glass and butyl rubber stopper.

Infusion bag: The container consists of an inner bag and an overpouch. An oxygen absorber and integrity indicator are placed between the inner bag and the overpouch. The inner bag is the primary container for Intralipid. The overpouch provides protection during storage by contributing with barrier properties towards water and oxygen to the
Intralipid container system. The oxygen absorber will absorb and bind oxygen remaining
between the inner bag and the overpouch. The integrity indicator will react with free oxygen and change from clear to black in case of a damaged overpouch.

The inner bag is made of a multilayer polymer film, alternatively Excel or Biofine.

- The Excel inner bag film consists of poly(propylene/ethylene) copolymer, thermoplastic elastomer (SEBS) and copolyester. The port system consists of poly(propylene/ethylene) copolymer and thermoplastic elastomer (SEBS). The infusion port is equipped with a polyolefin cap. The additive port is equipped with a synthetic polyisoprene (latex-free) stopper.

- The Biofine inner bag film consists of poly(propylene/ethylene) copolymer and thermoplastic elastomers (SEBS and SIS). The infusion and additive ports are made of polypropylene and a thermoplastic elastomer (SEBS) equipped with synthetic polyisoprene stoppers.

The oxygen barrier overpouch consists of polyolefin and polyethylene terephthalate or polyolefin, polyethylene terephthalate and poly(ethyl vinyl) alcohol (EVOH).

The oxygen absorber consists of iron powder in a polymer sachet.

The integrity indicator (Oxalert) consists of an oxygen sensitive solution in a polymer sachet.

Pack sizes

100 ml (10x100 ml)
250 ml (10x250 ml)
500 ml (12x500 ml)

6.6 Special precautions for disposal

Do not use if the package is damaged.

Infusion bag: The integrity indicator (Oxalert) should be inspected before removing the overpouch. If the indicator is black, oxygen has penetrated the overpouch and the product should be discarded.

Additions should be made aseptically. Single administration of electrolyte solutions to Intralipid should not be made. Only medicinal, nutritional or electrolyte solutions for which compatibility has been documented may be added as directed. Compatibility data are available from the manufacturer for a number of mixtures.

The left over contents of opened bottles / bags should be discarded and not saved for later use. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.
Apart from information provided elsewhere in the SPC, there are no special instructions on handling of the product.

Discard any unused portion.

Do not reconnect partially used bags.

7 MARKETING AUTHORISATION HOLDER

Fresenius Kabi Limited

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Manor Park

Runcorn

Cheshire

WA7 1NT

8. MARKETING AUTHORISATION NUMBER(S)

Intralipid 20% PL 08828/0110

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

19/03/2009

10 DATE OF REVISION OF THE TEXT

27/04/2016