Intralipid® 10% and 20%
Emulsion for Infusion

Trade name of the medicinal product
Intralipid 10%, Emulsion for Infusion
Intralipid 20%, Emulsion for Infusion

Qualitative and quantitative composition

Intralipid 10%
1000 ml of the emulsion contains: Purified soybean oil of 100 g, purified egg phospholipids, glycerol anhydrous, sodium hydroxide, water for injections
pH appr 8
Osmolality: 300 mosm/kg/water
Energy content: 4.6 MJ (1100 kcal) / 1000 ml
Organic phosphate content: 15 mmol / 1000ml

Intralipid 20%
1000 ml of the emulsion contains: Purified soybean oil of 200 g, purified egg phospholipids, glycerol anhydrous, sodium hydroxide, water for injections
pH appr 8
Osmolality: 350 mosm/kg/water
Energy content: 8.4 MJ (2000 kcal) / 1000 ml
Organic phosphate content: 15 mmol / 1000ml

PHARMACEUTICAL FORM
Emulsion for Infusion
White homogenous emulsion

CLINICAL PARTICULARS

Therapeutic Indications
INTRALIPID is indicated in patients needing intravenous nutrition to supply energy and essential fatty acids. INTRALIPID is also indicated in patients with essential fatty acid deficiency (EFAD) who cannot maintain or restore a normal essential fatty acid pattern by oral intake.

Posology and method of administration
The ability to eliminate INTRALIPID should govern the dosage and infusion rate. See below **Fat elimination.**

DOSAGE Intralipid 10%
1g triglycerides corresponds to 10 ml INTRALIPID 10%.

Adults. The recommended maximum dosage is 3 g triglycerides/ kg body weight/day. Within this upper limit, INTRALIPID can be given to contribute up to 70%

of the energy requirements, also in patients with highly increased energy requirements. The infusion rate for INTRALIPID 10% should not exceed 500 ml in 5 hours.

Neonates and infants. The recommended dosage range in neonates and infants is 0.5-4 g triglycerides/ kg bw/day. The rate of infusion should not exceed 0.17 g triglycerides/kg bw/hour (4 g in 24 hours). In prematures and low birthweight neonates, INTRALIPID should preferably be infused continuously over 24 hours. The initial dosage should be 0.5-1 g/kg bw/day followed by a successive increase by 0.5-1 g/kg bw/day up to 2g/kg bw/day. Only with close monitoring of serum triglyceride concentration, liver tests and oxygen saturation may the dosage be increased to 4 g/kg bw/day. The rates given are maximum rates and no attempt should be made to exceed these in order to compensate for missed doses. When used in neonates and children below 2 years, the solution (in bags and administration sets) should be protected from light exposure until administration is completed.

DOSAGE Intralipid 20%

1g triglycerides corresponds to 5 ml INTRALIPID 20%.

Adults. The recommended maximum dosage is 3 g triglycerides/ kg body weight/day. Within this upper limit, INTRALIPID can be given to contribute up to 70% of the energy requirements, also in patients with highly increased energy requirements. The infusion rate for INTRALIPID 20% should not exceed 500 ml in 5 hours.

Neonates and infants. The recommended dosage range in neonates and infants is 0.5-4 g triglycerides/ kg bw/day. The rate of infusion should not exceed 0.17 g triglycerides/kg bw/hour (4 g in 24 hours). In prematures and low birthweight neonates, INTRALIPID should preferably be infused continuously over 24 hours. The initial dosage should be 0.5-1 g/kg bw/day followed by a successive increase by 0.5-1 g/kg bw/day up to 2g/kg bw/day. Only with close monitoring of serum triglyceride concentration, liver tests and oxygen saturation may the dosage be increased to 4 g/kg bw/day. The rates given are maximum rates and no attempt should be made to exceed these in order to compensate for missed doses. When used in neonates and children below 2 years, the solution (in bags and administration sets) should be protected from light exposure until administration is completed.

Essential fatty acid deficiency (EFAD). To prevent or correct essential fatty acid deficiency, 4 to 8% of the nonprotein energy should be supplied as INTRALIPID to provide sufficient amounts of linoleic and linolenic acid. When EFAD is associated with stress, the amount of INTRALIPID needed to correct the deficiency may be substantially increased.

Administration. INTRALIPID may be infused into the same central or peripheral vein as carbohydrates/amino acid solutions by means of a Y-connector near infusion site.

INTRALIPID can also be given in a phthalate-free plastic bag as one part of an All in One admixture containing also carbohydrates, amino acids, electrolytes, vitamins and trace elements. The admixtures must be approved for physical stability according to Fresenius Kabi standards.

Fat Elimination

Adults. The ability to eliminate fat should be closely monitored in patients with conditions mentioned in section "Special warnings and special precautions for use", and in patients given Intralipid for more than one week. This is done by collecting a blood sample after a fat-free clearance period of 5-6 hours. Blood cells are then separated from plasma by centrifugation. If the plasma is opalescent, the infusion should be postponed. The sensitivity of this method is such that hypertriglyceridaemia can pass undetected. Therefore, it is recommended that serum triglyceride concentrations should be measured in patients who are likely to have impaired fat tolerance.

Neonates and infants. The ability to eliminate fat should be tested regularly in neonates and infants. Measuring serum triglyceride levels is the only reliable method.

Contra-indications

INTRALIPID is contraindicated in patients with acute shock and those with severe disturbances in lipid metabolism such as pathologic hyperlipemia. INTRALIPID is also contraindicated in patients with severe liver insufficiency, hemophagocytotic syndrome, hypersensitivity to egg-, soya- or peanut protein or to any of the active substances or excipients. INTRALIPID also should not be used in patients with acute myocardial infarction until the condition has stabilized.

Special warnings and special precautions for use

INTRALIPID should be given with caution in conditions of impaired lipid metabolism as in renal insufficiency, uncompensated diabetes mellitus, pancreatitis, impaired liver function, hypothyroidism (if hypertri-glyceridemic) and sepsis. If INTRALIPID is given to patients with these conditions, close monitoring of the serum triglyceride concentration is obligatory.

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.

INTRALIPID should be given with caution to neonates and prematures with hyperbilirubinemia and cases with suspected pulmonary hypertension. In neonates, particularly prematures on long term parenteral nutrition, platelet count, liver test and serum triglyceride concentration should be monitored. When used in neonates and children below 2 years, the solution (in bags and administration sets) should be protected from light exposure until administration is completed. Exposure of Intralipid to ambient light, especially after admixtures with trace elements and/or vitamins, generates peroxides and other degradation products that can be reduced by protection from light exposure.

INTRALIPID may interfere with certain laboratory measurements (bilirubin, lactate dehydrogenase, oxygen saturation, Hb etc) if blood is sampled before fat has been adequately cleared from the blood stream. Fat is cleared after a fat free interval of 5-6 hours in most patients.

Interaction with other medicaments and other forms of interaction

Some drugs, like insulin, may interfere with the body's lipase system. This kind of interaction seems, however, 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 clearance 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.

Pregnancy and lactation
No adverse reactions connected with pregnancy have been reported. Animal reproduction studies have not been carried out with INTRALIPID.

Nursing mothers: Caution should be exercised when INTRALIPID is administered to a nursing woman.

Effects on ability to drive and use machines
No effects on the ability to drive and operate machines are to be expected.

Adverse events
INTRALIPID infusion may cause a rise in body temperature (incidence <3%) and, less frequently, shivering, chills and nausea/vomiting (incidence <1%).

Reports of other adverse events in conjunction with INTRALIPID infusion are extremely rare, less than one report of a certain event per one million infusions.

Immediate or early adverse events. Hypersensitivity reactions (anaphylactic reaction, skin rash, urticaria), respiratory symptoms (e.g. tachypnea) and circulatory effects (e.g. hyper/hypotension) have been described. Haemolysis, reticulocytosis, abdominal pain, headache, tiredness and priapism have been reported.

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.

Delayed adverse events. Thrombocytopenia has been reported in association with prolonged treatment with INTRALIPID in infants. Transient increase in liver tests after prolonged intravenous nutrition with or without INTRALIPID have also been noted.

Impaired capacity to eliminate INTRALIPID may lead to the fat overload syndrome as a result of overdose but also at recommended rates of infusion in association with sudden change in the clinical condition such as renal function impairment or infection. Fat overload syndrome is characterized by hyperlipaemia, fever, fat-infiltration and disorders in various organs and coma. All symptoms are usually reversible if the infusion of INTRALIPID is discontinued.

Overdose
When fat emulsion is given in amounts exceeding the capacity of fat elimination the following symptoms may occur: hyperlipemia, hepatosplenomegaly, jaundice, hemolytic

anemia, prolonged clotting time and thrombocytopenia. All symptoms clear in days to weeks after cessation of fat infusion.

PHARMACOLOGICAL PROPERTIES

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 utilized. 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.

Pharmacokinetic properties

INTRALIPID is metabolised in a similar way to chylomicrons.

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.

PHARMACEUTICAL PARTICULARS

Incompatibilities

INTRALIPID can only be mixed with other medicinal products for which compatibility has been documented.

Shelf life

Shelf life in the product as packaged for sale. 24 months

Shelf life after first opening the container. The emulsion should be used directly due to the risk of microbiological contamination. Any unused emulsion should be discarded.

Shelf life after addition or mixing according to directions. When additions are made to infusion solution, the infusion should be completed within 24 hours.

Special precautions for storage

Store below 25°C. Do not freeze.

After addition of other nutritional elements
Mixing in plastic bag (phthalate free film): Mixtures aseptically prepared in a controlled and validated aseptic area should be used within 7 days after preparation.
The mixtures can be stored up to 6 days in a refrigerator (2-8°C) followed by an infusion period of up to 24 hours.

Nature and contents of container

Infusion bottle. Type II glass and butyl rubber stopper.

Pack sizes:
Intralipid 10% 100 ml, 500ml
Intralipid 20% 100 ml, 250 ml, 500 ml, 1000 ml

Excel bag. The excel bag consist of an inner bag (primary package) with an overpouch. An oxygen absorber and an integrity indicator (Oxalert™) are placed between the innerbag and the overpouch.
The innerbag consists of a poly (propylene/ethylene) copolymer, a thermoplastic elastomer and a co-polyester. The overpouch, the oxygen absorber and the integrity indicator should be discarded after opening of the overpouch. The integrity indicator (Oxalert™) will react with free oxygen and change colour in case of a damage in the overpouch.

Pack sizes:
Intralipid 10% 100 ml, 500ml
Intralipid 20% 100 ml, 250 ml, 500 ml

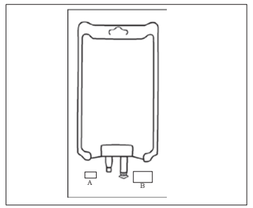
Not all presentations are available.

Instructions for use/handling
When used in neonates and children below 2 years, the solution (in bags and administration sets) should be protected from light exposure until administration is completed.
Do not use if package is damaged. For Excel bag: After inspection of the integrity indicator, the overpouch has to be removed.
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.

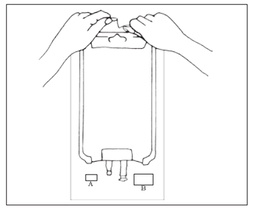
DATE OF REVISION OF THE TEXT
May 2011 (Singapore)

Fresenius Kabi AB, 751 74 Uppsala, Sweden

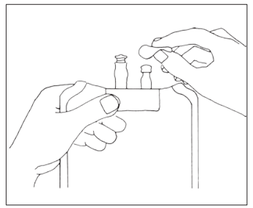
Instructions for use - Fresenius Kabi infusion bag



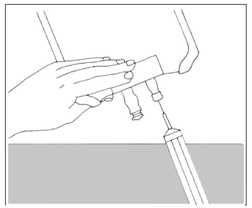
1. The integrity indicator (Oxalert™) A should be inspected before removing the overpouch. If the indicator is black the overpouch is damaged and the product should be discarded.



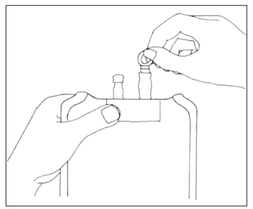
2. Remove the overwrap by tearing at the notch and pulling down along the container. The Oxalert™ sachet A and the oxygen absorber B should be disposed.



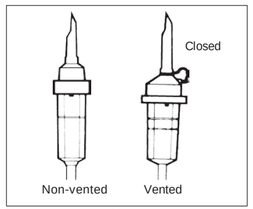
3. If additions are to be made, swab injection site.



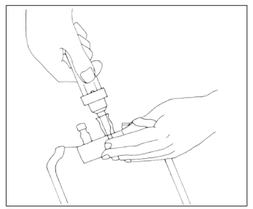
4. Place the container on a table and support the base of the medication port. Fully insert the needle through centre of injection site. Mix thoroughly by inverting container several times.



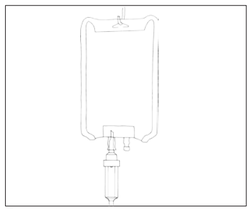
5. Remove set port cover by lifting ring with thumb and forefinger and pulling upwards.



6. Use a non-vented infusion set or close the air vent on a vented set. Follow the instructions for use for the infusion set.



7. The bag should be with the port side up when the infusion set is attached. Insert the spike straight into the set port. Twist and push the spike through the diaphragm. The spike should be fully inserted to ensure its retention.



8. To hang the bag, invert and place hanger through container notch.