For the use of a registered medical practitioner or a Hospital or a Laboratory only

Intravenous Fat Emulsion

NIRPID®*

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DESCRIPTION:

NIRPID®* is a stable fat emulsion prepared from Soybean Oil, Egg Lecithin, Glycerol and Water For Injection. Fat emulsion has the advantage of having high caloric yield. NIRPID®* is also isotonic with blood and hence can be infused peripherally.

The soybean oil of NIRPID®* provides essential fatty acid which helps to avoid essential fatty acid deficiency and its associated biochemical changes and clinical manifestation like scaly skin, growth retardation, sparse hair growth & delayed wound healing.

A Parenteral feeding regimen, which contains carbohydrates, amino acid and fats provides a balanced metabolic load. Thus fat emulsions are indispensable unless fats are contraindicated.

COMPOSITION:

NIRPID®* is an intravenous fat emulsion and has the following Composition

Each 100 mL (of emulsion) Contains

	NIRPID 20%™*	**NIRPID 10%™***
Soyabean Oil IP	20.00 gm	10.00 gm
Egg Lecithin	1.20 gm	1.20 gm
Glycerol IP	2.25 gm	2.25 gm
Water for Injections IP	q. s.	q. s.
Energy content Kcal/L	2000	1100
Osmolarity mOsmol/L	279	300

PHARMACOLOGY:

NIRPID®* is eliminated from the circulation via the same metabolic pathway as chylomicrons. Following IV injection, a transient hyperlipidemia occurs as the fat emulsion particles breakdown and release triglycerides. These exogenous triglycerides are hydrolyzed by lipoprotein lipase, a capillary endothelial enzyme that also metabolizes endogenous serum triglycerides. Hence free Glycerol, free fatty acid and other glycerides are formed with adequate tissue perfusion. Intravenous fat emulsion are maximally cleared at the rate of 2 - 4 g/kg/ day.

The free fatty acids either enter the tissue or circulate in the plasma bound to albumin. Circulating free fatty acids are oxidized or converted to low-density lipo proteins that reenter the blood stream hence NIRPID®* is used as a source of energy. Choline helps to prevent deposition of the fats in the liver. Glycerol is oxidized to give energy and carbon dioxide or is used for synthesis of body fats.

INDICATIONS:

NIRPID®* Provides energy in

- Pre & Post-operative nutritional disturbances
- Cancer & associated Cachexia
- Intravenous nutrition in Burns

• G.I.Tract diseases
• Malabsorption
• Impaired renal function
• Prolonged unconsciousness - Head injury, Poisoning

CONTRAINDICATIONS:
Disturbances of fat metabolism
Advance liver disease
Acute shock
Egg allergies
Traumatic brain injury
Coagulation disorders
Pulmonary hypertension

WARNING:
NIRPID®* should be given with caution to neonates and premature with hyperbillirubinemia and in cases with suspected pulmonary hypertension. In neonates particularly premature or long-term parenteral nutrition platelets counts, liver test and serum triglycerides concentration should be monitored.

Deaths in preterm infants after infusion of intravenous fat emulsion have been reported in the medical literature. Autopsy findings included intravascular fat accumulation in the lungs. Treatment of premature and low birth weight infants with intravenous fat emulsion must be based upon careful benefit-risk assessment. Strict adherence to the recommended total daily dose is mandatory; hourly infusion rate should be as slow as possible in each case and should not in any case exceed 1 g fat/kg in 4 hours. Premature and small for gestational age infants have poor clearance of intravenous fat emulsion and increased free fatty acid plasma levels following fat emulsion infusion; therefore, serious consideration must be given to administration of less than the maximum recommended doses in these patients in order to decrease the likelihood of intravenous fat overload. The infant's ability to eliminate the infused fat from the circulation must be carefully monitored (such as serum triglycerides and/or plasma free fatty acid levels). The lipemia must clear between daily infusions.

PRECAUTION:
Before infusion the patient's liver function, haemogram, blood coagulation, platelets count and plasma lipid profile must be monitored. The lipid must be cleared from plasma after daily infusion.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Studies with NIRPID®* have not been performed to evaluate carcinogenic potential, mutagenic potential, or effects on fertility.

Pregnancy Category C: Animal reproduction studies have not been conducted with NIRPID®*. It is also not known whether NIRPID®* can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. NIRPID®*should be given to a pregnant woman only if clearly needed.

Nursing Mothers: Caution should be exercised when NIRPID®* is administered to a nursing woman.

CAUTION:
After the infusion is initiated, the patient is closely observed for sings of acute hypersensitivity characterized by chills, palpitation, dyspnea. These reactions may be associated with faster flow rate and this occurrence necessitates a reduction in flow rate.

Do not store partially used bottles.
Do not use the fluid if any separation of phases of the emulsion is visible.
Emulsion should not be mixed with electrolytes or other additives.
Poor maternal weight gain increases the risk of delivery of a low birth weight infant, thus increasing the risk of neonatal death. Fat emulsion may be useful for preventing such nutritional deficits. Successful and safe administration of lipid emulsion in pregnant women has been reported.

ADVERSE REACTIONS:
Rare adverse reactions occurred during infusion are of two types.
Immediate type reactions include febrile response, chills, shivering, pain in chest and back, palpitations, dizziness, tachypnea, hyper/hypotension, transient increase in liver enzymes. Delayed type reactions include hepatomegaly, jaundice due to central lobular cholestasis, splenomegaly, thrombocytopenia, leucopenia. Too rapid infusions can lead to dilution of serum electrolytes, fat overload, fluid overload metabolic acidosis and pulmonary oedema. If fat overload occurs during the infusion it must be postponed. Fat overload can be detected by milky appearance of plasma.

DOSAGE:
Adult Patients
The initial rate of infusion of NIRPID 20%™* should be 0.5 ml/minute and NIRPID 10%™* should be 1 ml/minute for the first 15 to 30 minutes of infusion. If no untoward reactions occur the infusion rate can be increased to 1 ml/minute for NIRPID 20%™* and 2 ml/minute for NIRPID 10%™*. Not more than 500 ml of NIRPID®* should be infused into adults on the first day of therapy. If the patient has no untoward reactions, the dose can be increased on the following day. The daily dosage should not exceed 2.5 g of fat/kg BW (12.5 ml of NIRPID 20%™* per kg or 25 ml of NIRPID 10%™* per kg). NIRPID®* (10% & 20%) should make up no more than 60% of the total caloric input to the patient. Carbohydrate and a source of amino acids should comprise the remaining caloric input.

NIRPID®* should be given to a pregnant woman only if clearly needed.

Pediatric Patients
The dosage for premature infants starts at 0.5 g fat/kg body weight/24 hours (2.5 ml NIRPID 20%™* or 5 ml NIRPID 10%™*) and may be increased in relation to the infant's ability to eliminate fat. The maximum dosage recommended by the American Academy of Pediatrics is 3 g fat/kg/24 hours. The initial rate of infusion in older pediatric patients should be no more than 0.05 ml/minute for NIRPID 20%™* and 1 ml/minute for the NIRPID 10%™* for the first 10 to 15 minutes. If no untoward reactions occur, the rate can be changed to permit infusion of 0.5 ml of NIRPID 20%™*/kg/hour or 1 ml of
NIRPID 10%™*/hour. The daily dosage should not exceed 3 g of fat/kg BW. NIRPID®* should make up no more than 60% of the total caloric input to the patient. Carbohydrate and a source of amino acids should comprise the remaining caloric input.
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 NIRPID®* (10% & 20%) 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.

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.

Essential Fatty Acid Deficiency
When NIRPID®* is administered to correct essential fatty acid deficiency, eight to ten percent of the caloric input should be supplied by NIRPID®* in order to provide adequate amounts of linoleic and linolenic acids. When EFAD occurs together with stress, the amount of NIRPID®* needed to correct the deficiency may be increased.

INFUSION RATE:
The Infusion rate of NIRPID 20%™*500ml for initial 15-30 min. for adults should not exceed 0.5 ml/min. If no adverse reactions are observed then subsequent infusion can be given over a period of 8 to 12 hours.
Infants, the infusion should be initiated a rate of 0.1ml/min. for 15 min If no adverse reactions are observed, subsequent infusion can be given at not more than 50ml of NIRPID 20%™* per hours.
The Infusion rate of NIRPID 10%™* for initial 15-30 min. for adults should not exceed 1 ml/min. lf no adverse reactions are observed then subsequent infusion can be given over a period of 4 to 6 hours. Infants, the infusion should be Initiated at a rate of 0.1ml/min. for 15 min. If no adverse reactions are observed, subsequent infusion can be given at not more than 50ml of NIRPID 10%™* per hour.

ADMINISTRATION:
See MIXING GUIDELINES AND LIMITATIONS section for information regarding mixing this fat emulsion with other parenteral fluids. NIRPID®* can be infused into the same central or peripheral vein as carbohydrate/amino acids solutions by means of a Y-connector near the infusion site. This allows for mixing of the emulsion immediately before entering the vein or for alternation of each parenteral fluid. If infusion pumps are used, flow rates of each parenteral fluid should be controlled with a separate pump. Fat emulsion may also be infused through a separate peripheral site. Filters of less than 1.2 micron pore size must not be used with NIRPID®*. Conventional administration sets contain polyvinyl chloride (PVC) components that have DEHP (diethyl hexyl phthalate) as a plasticizer. Fat-containing fluids such as NIRPID®* extract DEHP from these PVC components and it may be advisable to consider infusion of NIRPID®* through a non-DEHP administration set.

MIXING GUIDELINES AND LIMITATIONS:
The following proper mixing sequence must be followed to minimize pH related problems by ensuring that typically acidic Dextrose Injections are not mixed with lipid emulsions alone:
1. Transfer Dextrose Injection to the TPN Admixture Container
2. Transfer Amino Acid Injection
3. Transfer NIRPID 20%™* or NIRPID 10%™* (A 20% or 10% Intravenous Fat Emulsion)

Note: Amino Acid Injection, Dextrose Injection and NIRPID®* may be simultaneously transferred to the admixture container. Admixing should be accompanied by gentle agitation to avoid localized concentration effects. These admixtures should be used promptly.
It is essential that the admixture be prepared using strict aseptic techniques as this nutrient mixture is a good growth medium for microorganisms.
Additives other than those named above may be incompatible. Complete information is not available.
Those additives known to be incompatible should not be used.

Mix thoroughly when additives have been introduced. Do not store solutions containing additives (e.g., vitamins and minerals).
Additives must not be added directly to NIRPID®* and in no case should NIRPID®* be added to the TPN container first. Bags should be shaken gently after each addition to minimize localized concentration.
The prime destabilizers of emulsions are excessive acidity (low pH) and inappropriate electrolyte content. Careful consideration should be given to additions of divalent cations (Ca++ and Mg++) which have been shown to cause emulsion instability.
should be inspected carefully for "breaking or oiling out" of the emulsion. "Breaking or oiling out" is described as the separation of the emulsion and can be visibly identified by a yellowish streaking or the accumulation of yellowish droplets in the admixed emulsion. The admixture should also be examined for particulates. The admixture must be discarded if any of the above is observed.

OVER DOSAGE:
If fat overload occurs during therapy, the fat infusion must be stopped immediately. Further therapy should be initiated with appropriate corrective measures.

STORAGE:
Store below 25° C. Do not freeze.

PRESENTATION:
NIRPID 10%™*- In 100 mL, 250 mL, 500 mL and 1000mL glass bottle.
NIRPID 20%™*- In 100 mL, 250 mL, 500 mL and 1000mL glass bottle.

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Manufactured in India by:
Aculife Healthcare Pvt. Ltd.
Sachana, Gujarat 382150, India.

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