Bipacksedel **335 894** (ersätter 335 774)
Tryckspecifikation

Format:	630 x 210 mm
Färger:	PMS svart
Utskrift:	anpassat till A3

3:e korr. 15-06-09
Johanna Eriksson, 018 64 40 46

Intralipid® 30%

A 30% I.V. Fat Emulsion

FRESENIUS KABI

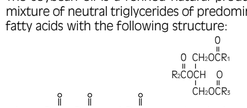
Pharmacy Bulk Package
Not For Direct Infusion

DESCRIPTION

Intralipid® 30% (A 30% I.V. Fat Emulsion) Pharmacy Bulk Package is a sterile, non-pyrogenic fat emulsion intended as a source of calories and essential fatty acids for use in a pharmacy admixture program. It is made up of 30% Soybean Oil, 1.2% Egg Yolk Phospholipids, 1.7% Glycerin, and Water for Injection. In addition, sodium hydroxide has been added to adjust the pH so that the final product pH is 8. pH range is 6 to 8.9.

Intralipid® 30% Pharmacy Bulk Package is not intended for direct infusion. It is a sterile dosage form which contains several single doses for use in the preparation of three-in-one or total nutrient admixtures (TNAs) in a pharmacy admixture program.

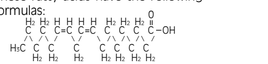
The soybean oil is a refined natural product consisting of a mixture of neutral triglycerides of predominantly unsaturated fatty acids with the following structure:



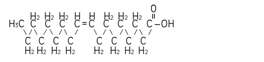
where R_1C-, R_2C- and R_3C- are saturated and unsaturated fatty acid residues.[1]

The major component fatty acids are linoleic acid (44-62%), oleic acid (19-30%), palmitic acid (7-14%), α-linolenic acid (4-11%) and stearic acid (1.4-5.5%).[1] These fatty acids have the following chemical and structural formulas:

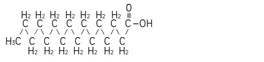
Linoleic acid
$C_{18}H_{32}O_2$



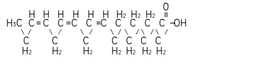
Oleic acid
$C_{18}H_{34}O_2$



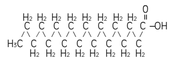
Palmitic acid
$C_{16}H_{32}O_2$



α-Linolenic acid
$C_{18}H_{30}O_2$

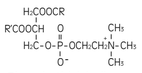


Stearic acid
$C_{18}H_{36}O_2$

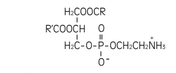


Purified egg phosphatides are a mixture of naturally occurring phospholipids which are isolated from the egg yolk. These phospholipids have the following general structure:

R_1C- and R_2C contain saturated and unsaturated fatty acids that abound in neutral fats. R_3 is primarily either the choline or the ethanolamine ester of phosphoric acid.



Phosphatidylcholine



Phosphatidylethanolamine

Glycerin is chemically designated $C_3H_8O_3$ and is a clear colorless, hygroscopic syrupy liquid. It has the following structural formula:

Intralipid® 30% (A 30% I.V. Fat Emulsion) has an osmolality of approximately 310 mOsmoL/kg water (which represents 200 mOsmoL/L of emulsion) and contains emulsified fat particles of approximately 0.5 micron size.

The total caloric value, including fat, phospholipid and glycerin, is 3.0 kcal per mL of Intralipid® 30%. The phospholipids present contribute 47 milligrams or approximately 1.5 mmol of phosphorus per 100 mL of the emulsion.

The primary plastic container (Biofine™), is made from multilayered film specifically designed for parenteral nutrition drug products. The film is polypropylene based comprising three co-extruded layers. It contains no plasticizers and exhibits virtually no leachables. The container does not contain DEHP (di(2-ethylhexyl)phthalate) or PVC. This product is not made with natural rubber latex. The container is nontoxic and biologically inert.

The container-emulsion unit is a closed system and is not dependent upon entry of external air during administration. The container is overwrapped to provide protection from the physical environment and to provide an additional moisture barrier when necessary.

CLINICAL PHARMACOLOGY

Intralipid® is metabolized and utilized as a source of energy causing an increase in heat production, decrease in respiratory quotient and increase in oxygen consumption. The infused fat particles are cleared from the blood stream in a manner thought to be comparable to the clearing of chylomicrons.

Intralipid® will prevent the biochemical lesions of essential fatty acid deficiency (EFAD), and correct the clinical manifestations of the EFAD syndrome.

INDICATIONS AND USAGE

Intralipid® 30% Pharmacy Bulk Package is indicated for use in a pharmacy admixture program for the preparation of three-in-one or total nutrient admixtures (TNAs) to provide a source of calories and essential fatty acids for patients requiring parenteral nutrition for extended periods of time (usually for more than 5 days) and as a source of essential fatty acids for prevention of EFAD.

CONTRAINDICATIONS

INTRALIPID® 30% PHARMACY BULK PACKAGE IS NOT INTENDED FOR DIRECT INTRAVENOUS ADMINISTRATION. DILUTING INTRALIPID® 30% TO A 10% OR 20% CONCENTRATION WITH AN INTRAVENOUS FLUID SUCH AS NORMAL SALINE OR OTHER DILUENT DOES NOT PRODUCE A DILUTION THAT IS EQUIVALENT IN COMPOSITION TO INTRALIPID® 10% OR 20% I.V. FAT EMULSIONS, AND SUCH A DILUTION SHOULD NOT BE GIVEN BY DIRECT INTRAVENOUS ADMINISTRATION (FOR EXAMPLE, THROUGH A Y-CONNECTOR).

The administration of Intralipid® is contraindicated in patients with disturbances of normal fat metabolism such as pathologic hyperlipemia, lipoid nephrosis or acute pancreatitis if accompanied by hyperlipidemia. Intralipid® 30% (A 30% I.V. Fat Emulsion) is not intended for direct intravenous infusion.

WARNINGS

Deaths in preterm infants after infusion of intravenous fat emulsion have been reported in the medical literature.[2] 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 the total fat should not in any case exceed 1 g fat/kg in four 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.

Caution should be exercised in administering of Intralipid® 30% to patients with severe liver damage, pulmonary disease, anemia or blood coagulation disorders, or when there is danger of fat embolism.

WARNING: This product contains aluminum that may be toxic. Aluminum may reach toxic levels with prolonged parenteral administration if kidney function is impaired. Premature neonates are particularly at risk because their kidneys are immature, and they require large amounts of calcium and phosphate solutions, which contain aluminum.

Research indicates that patients with impaired kidney function, including premature neonates, who receive parenteral levels of aluminum at greater than 4 to 5 mcg/kg/day accumulate aluminum at levels associated with central nervous system and bone toxicity. Tissue loading may occur at even lower rates of administration.

PRECAUTIONS

When Intralipid® is administered, the patients capacity to eliminate the infused fat from the circulation must be monitored by use of an appropriate laboratory determination of serum triglycerides. Overdosage must be avoided.

During long term intravenous nutrition with Intralipid®, liver function tests should be performed. If these tests indicate that liver function is impaired, the therapy should be withdrawn.

Frequent (some advise daily) platelet counts should be done in neonatal patients receiving parenteral nutrition with Intralipid®.

Drug product contains no more than 25 mcg/L of aluminum.

Carcinogenesis, Mutagenesis, Impairment of Fertility. Studies with Intralipid® 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 Intralipid®. It is also not known whether Intralipid® can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Intralipid® should be given to a pregnant woman only if clearly needed.

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

Pediatric Use: See DOSAGE AND ADMINISTRATION.

AVOID OVERDOSAGE ABSOLUTELY.

ADVERSE REACTIONS

The adverse reactions observed can be separated into two classes:

1. Those more frequently encountered are due either to a) contamination of the intravenous catheter and result in sepsis, or to b) vein irritation by concurrently infused hypertonic solutions and may result in thrombophlebitis. These adverse reactions are inseparable from the hyperalimentation procedure with or without Intralipid®.
2. Less frequent reactions more directly related to Intralipid® are: a) immediate or early adverse reactions, each of which has been reported to occur in clinical trials, in an incidence of less than 1%: dyspnea, cyanosis, allergic reactions, hyperlipemia, hypercoagulability, nausea, vomiting, headache, flushing, increase in temperature, sweating, sleepiness, pain in the chest and back, slight pressure over the eyes, dizziness, and irritation at the site of infusion, and, rarely, thrombocytopenia in neonates; b) Delayed adverse reactions such as hepatomegaly, jaundice due to central lobular cholestasis, splenomegaly, thrombocytopenia, leukopenia, transient increases in liver function tests, and overloading syndrome (focal seizures, fever, leukocytosis, hepatomegaly, splenomegaly and shock).

The deposition of a brown pigmentation in the reticuloendothelial system, the so-called "intravenous fat pigment," has been reported in patients infused with Intralipid®. The causes and significance of this phenomenon are unknown.

OVERDOSAGE

In the event of fat overload during therapy, stop the infusion containing Intralipid® 30% (A 30% I.V. Fat Emulsion) until visual inspection of the plasma, determination of triglyceride concentrations, or measurement of plasma light-scattering activity by nephelometry indicates the lipid has cleared. Re-evaluate the patient and institute appropriate corrective measures. See WARNINGS and PRECAUTIONS.

DOSAGE AND ADMINISTRATION

Intralipid® 30% (A 30% I.V. Fat Emulsion) Pharmacy Bulk Package should be administered only as a part of a three-in-one or total nutrient admixture via peripheral vein or by central venous infusion.

Directions For Proper Use of Pharmacy Bulk Package

INTRALIPID® 30% (A 30% I.V. Fat Emulsion) PHARMACY BULK PACKAGE IS NOT INTENDED FOR DIRECT INFUSION. The container closure may be penetrated only once using a suitable sterile transfer device or dispensing set which allows measured dispensing of the contents. The Pharmacy Bulk Package is to be used only in a suitable work area such as a laminar flow hood (or an equivalent clean air compounding area). Once the closure is penetrated, the contents should be dispensed as soon as possible; the transfer of contents to suitable TPN admixture containers must be completed within 4 hours of closure penetration. The bag should be stored below 25°C (77°F) after the closure has been entered.

Admixtures made using Intralipid 30% should be used promptly. See MIXING GUIDELINES AND LIMITATIONS section for admixture storage recommendations.

Adult Patients

The initial infusion rate of the nutrient admixture in adults should be the equivalent of 0.1 g fat/minute for the first 15 to 30 minutes of infusion. If no untoward reactions occur (see ADVERSE REACTIONS section), the infusion rate of the nutrient admixture can be increased to be equivalent to 0.2 g fat/minute. For adults, the admixture should not contain more than 330 mL of Intralipid® 30% 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 of body weight (8.3 mL of Intralipid® 30% per kg). Intralipid® 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.

Pediatric Patients

The dosage for premature infants starts at 0.5 g fat/kg body weight/24 hours (1.7 mL) Intralipid® 30% 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.[3]

The initial rate of infusion of the nutrient admixture in older pediatric patients should be no more than 0.01 g fat/minute for the first 10 to 15 minutes. If no untoward reactions occur, the rate can be changed to permit infusion of 0.1 g of fat/kg/hour. The daily dosage should not exceed 3 g of fat/kg of body weight.[3] Intralipid® 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.

Essential Fatty Acid Deficiency

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

Administration

See MIXING GUIDELINES AND LIMITATIONS section for information regarding mixing this fat emulsion with other parenteral fluids. INTRALIPID® 30% (A 30% I.V. Fat Emulsion) is not for direct infusion. It must be infused as part of an admixture into a central or peripheral vein.

The flow rate of the admixture should be controlled with an infusion pump. Use a 1.2 micron filter with admixtures containing Intralipid® 30%. Filters of less than 1.2 micron pore size must not be used.

Conventional administration sets and TPN pooling bags contain polyvinyl chloride (PVC) components that have DEHP (di(2-ethylhexyl) phthalate) as a plasticizer. Fat-containing fluids such as Intralipid® extract DEHP from these PVC components. Therefore it may be advisable to use a non-DEHP administration set for infusing admixtures which contain Intralipid®.

Do not use any bag in which there appears to be an oiling out on the surface of the emulsion.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

MIXING GUIDELINES AND LIMITATIONS

INTRALIPID® 30% PHARMACY BULK PACKAGE IS NOT INTENDED FOR DIRECT INFUSION. It must be combined with total parenteral nutrition (TPN) fluids so that the resulting admixture has a final concentration of not more than 20% fat (0.2 g fat per mL of admixture). The following table may be used as a guide:

Volume of Intralipid® 30%		Required Minimum Volume of Dextrose/ Amino Acid Solutions		Final Volume of Admixture	Final fat Concentration
1 mL	+	0.5 mL	=	1.5 mL	20%
100 mL	+	50 mL	=	150 mL	20%
250 mL	+	125 mL	=	375 mL	20%
500 mL	+	250 mL	=	750 mL	20%

Because of the potential for life threatening events, caution should be taken to ensure that precipitates have not formed in any parenteral nutrition mixture. Perform all manipulations in a suitable work area, such as a laminar flow hood.

Failure to follow the Mixing Guidelines and Limitations below, including recommended storage temperature, storage time, order of mixing, etc., may result in an unstable admixture.

Intralipid® 30% (A 30% I.V. Fat Emulsion) may be mixed with Amino Acid and Dextrose Injections where compatibility have been demonstrated. Additives known to be incompatible should not be used. Please consult with pharmacist. If, in the informed judgment of the physician, it is deemed advisable to introduce additives, use aseptic technique. Mix thoroughly when additives have been introduced. Do not store solutions containing additives (e.g., Vitamins and Minerals).

When being mixed 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 Intralipid® 30% (A 30% I.V. Fat Emulsion)

Note: Amino Acid Injection, Dextrose Injection and Intralipid® may be simultaneously transferred to the admixture container. Admixing should be accompanied by gentle agitation to avoid localized concentration effects.

Additives must not be added directly to Intralipid® and in no case should Intralipid® be added to the TPN container first. Bags should be shaken gently after each addition to minimize localized concentration.

If the admixture is not used immediately, the in-use storage time and conditions prior to use are the responsibility of the user and should normally not be longer than 24 hours at 2-8°C. After removal from storage at 2-8°C, the admixture should be infused within 24 hours.

It is essential that the admixture be prepared using strict aseptic techniques as this nutrient mixture is a good growth medium for microorganisms.

Supplemental electrolytes, trace metals or multivitamins may be required in accordance with the prescription of the attending physician.

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. Amino acid solutions exert a buffering effect protecting the emulsion. The admixture 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.

HOW SUPPLIED

Intralipid® 30% (A 30% I.V. Fat Emulsion) is supplied as a sterile emulsion in a Pharmacy Bulk Package in the following fill sizes:

500 mL: 0338-0520-13

STORAGE

Intralipid® 30% should not be stored above 25°C (77°F). Do not freeze Intralipid® 30%. If accidentally frozen, discard the bag.

REFERENCES

1. Padley FB: "Major Vegetable Fats," The Lipid Handbook (Gunstone FD, Harwood JL, Padley FB, eds.), Chapman and Hall Ltd., Cambridge, UK (1986), pp. 88-9.
2. Levene MI, Wigglesworth JS, Desai R: Pulmonary fat accumulation after Intralipid® infusion in the preterm infant. Lancet 1980; 2(8199):815-8.
3. American Academy of Pediatrics: Use of intravenous fat emulsion in pediatric patients. Pediatrics 1981; 68:5(Nov) 738-43.

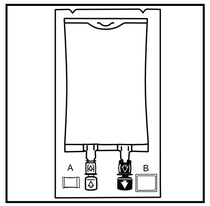
(Rev May 2015)

Manufactured for
Baxter Healthcare Corporation
Deerfield, IL 60015 USA

Manufactured by
Fresenius Kabi,
Uppsala, Sweden

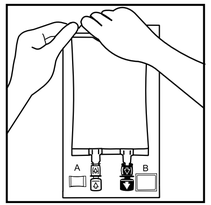
Instruction for Use - Intralipid® 30% Pharmacy Bulk Package Container

1.



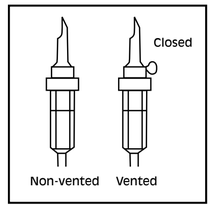
1. The integrity indicator (Oxalert™) **A** should be inspected before removing the overwrap. If the indicator is black the overwrap is damaged and the product should be discarded.

2.



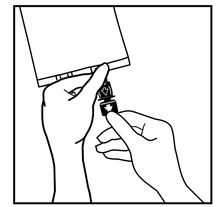
2. Remove the overwrap by tearing at the notch and pulling down along the container. The Oxalert™ sachet **A** and the oxygen absorber **B** should be disposed.

3.



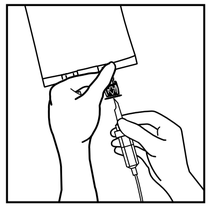
3. Use a non-vented infusion set or close the air vent on a vented set. Follow the instructions for use for the infusion set. Use a spike with diameter of 5.6 +/- 0.1 mm.

4.



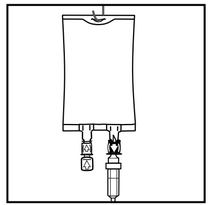
4. Break off the tamper-evident arrow flag from the blue infusion port.

5.



5. Hold the base of the infusion port. Insert the spike through the infusion port, by rotating your wrist slightly until the spike is inserted.

6.



6. Hang the bag in the hanger cut and start transfer to the compounding bag.

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