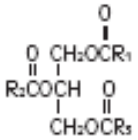
Intralipid® 10% (A 10% I.V. Fat Emulsion)

DESCRIPTION

Intralipid® 10% (A 10% Intravenous Fat Emulsion) is a sterile, non-pyrogenic fat emulsion prepared for intravenous administration as a source of calories and essential fatty acids. It is made up of 10% Soybean Oil, 1.2% Egg Yolk Phospholipids, 2.25% 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.

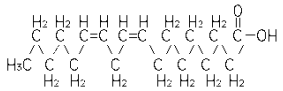
The soybean oil is a refined natural product consisting of a mixture of neutral triglycerides of predominantly unsaturated fatty acids with the following structure:



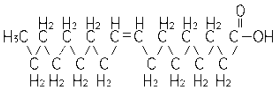
where R_1C-, R_2C- and R_3C- are saturated and unsaturated fatty acid residues.

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:

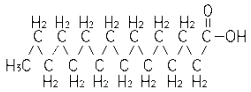
Linoleic acid
$C_{18}H_{32}O_2$



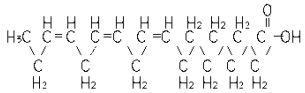
Oleic acid
$C_{18}H_{34}O_2$



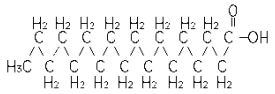
Plamitic acid
$C_{16}H_{32}O_2$



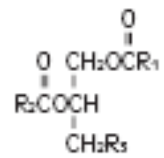
α-Linolenic acid
$C_{18}H_{30}O_2$



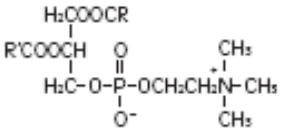
Stearic acid
$C_{18}H_{36}O_2$



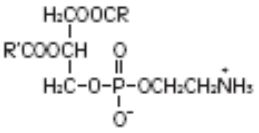
Purified egg phosphatides are a mixture of naturally occurring phospholipids which are isolated from the egg yolk. These phospholipids have the following general structure:



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

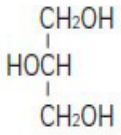


Phosphatidylcholine



Phosphatidylethanolamine

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



Intralipid 10% (A 10% Intravenous Fat Emulsion) has an osmolality of approximately 300 mOsmol/kg water (which represents 260 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 1.1 kcal per mL of Intralipid 10%. 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), PVC. The container is nontoxic and biologically inert. This product is not made with natural rubber latex.

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 10% 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 10% will prevent the biochemical lesions of essential fatty acid deficiency (EFAD) and correct the clinical manifestations of the EFAD syndrome.

INDICATIONS AND USAGE

Intralipid® 10% is indicated as 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 10% is contraindicated in patients with:

- Disturbances of normal fat metabolism such as pathologic hyperlipemia, lipoid nephrosis or acute pancreatitis if accompanied by hyperlipidemia.
- Known hypersensitivity to egg, soybean, peanut or any of the active ingredients or excipients of Intralipid 10%.

WARNINGS

Clinical Decompensation with Rapid Infusion of Intravenous Lipid Emulsions in Neonates and Infants

In the postmarketing setting, serious adverse reactions including acute respiratory distress, metabolic acidosis, and death have been reported in neonates and infants after rapid infusion of intravenous lipid emulsions. Hypertriglyceridemia was commonly reported.

Strictly adhere to the recommended total daily dosage; the hourly infusion rate should not exceed 1.0 mL/kg/hour. (see DOSAGE AND ADMINISTRATION section)

Preterm and small for gestational age infants have poor clearance of intravenous lipid emulsion and increased free fatty acid plasma levels following lipid emulsion infusion.

Carefully monitor the infant's ability to eliminate the infused lipids from the circulation (e.g., measure serum triglycerides and/or plasma free fatty acid levels). If signs or poor clearance of lipids from the circulation occur, stop the infusion and initiate a medical evaluation. (see PRECAUTIONS and OVERDOSAGE sections)

Parenteral Nutrition-Associated Liver Disease and Other Hepatobiliary Disorders

Risk of Parenteral Nutrition-Associated Liver Disease

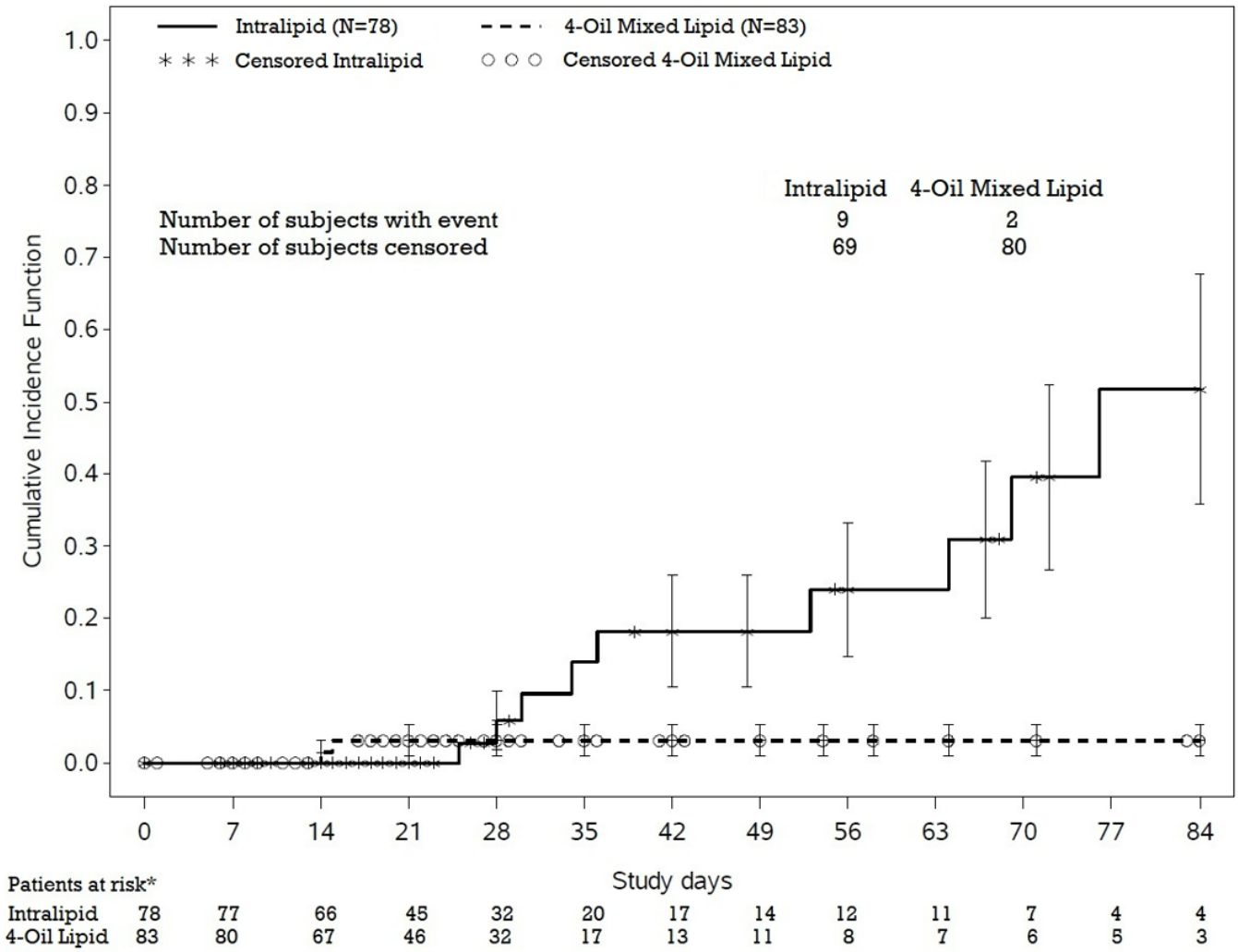
Parenteral nutrition-associated liver disease (PNALD), also referred to as intestinal failure-associated liver disease (IFALD), can present as cholestasis or hepatic steatosis, and may progress to steatohepatitis with fibrosis and cirrhosis (possibly leading to chronic hepatic failure). The etiology of PNALD is multifactorial; however, intravenously administered phytosterols (plant sterols) contained in plant-derived lipid emulsions, including Intralipid, have been associated with development of PNALD.

In a randomized active-controlled, double-blind, parallel-group, multi-center study that included 152 neonates and 9 patients ranging in age from 29 to 153 days who were expected to require PN for at least 28 days, parenteral nutrition-associated cholestasis (PNAC), a precursor to PNALD, developed more frequently in Intralipid-treated patients than in patients treated with a 4-oil mixed lipid emulsion.

PNAC (defined as direct bilirubin >2mg/dl with a second confirmed elevation >2mg/dl at least 7 days later) occurred in 11.5% (9/78) in Intralipid-treated patients and 2.4% (2/83) of patients treated with a 4-oil mixed lipid emulsion. Most PNAC events occurred in patients who were treated for longer than 28 days.

The estimated cumulative incidence of PNAC is shown in the Kaplan-Meier cumulative incidence curve in Figure 1.

Figure 1: Cumulative Incidence Curve of Time to Parenteral Nutrition-Associated Cholestasis (PNAC) with Standard Error Bars



*There is increasing uncertainty in the estimate of the cumulative incidence as fewer patients are at risk.

Monitor liver tests in patients treated with Intralipid and consider discontinuation or dosage reduction if abnormalities occur.

Other Hepatobiliary Disorders

Hepatobiliary disorders including cholecystitis and cholelithiasis have developed in some PN-treated patients without preexisting liver disease.

Monitor liver tests when administering Intralipid. Patients developing signs of hepatobiliary disorders should be assessed early to determine whether these conditions are related to Intralipid use.

Hypersensitivity Reactions

Intralipid 10% contains soybean oil and egg phospholipids, which may cause hypersensitivity reactions. Cross reactions have been observed between soybean and peanut. In postmarketing experience, anaphylaxis has been reported following Intralipid administration (See ADVERSE REACTIONS section).

Intralipid 10% is contraindicated in patients with known hypersensitivity to egg, soybean, peanut or any of the active or inactive ingredients in Intralipid (See CONTRAINDICATIONS section). Monitor patients during and after infusion. If a hypersensitivity reaction occurs, stop infusion of Intralipid 10% immediately and initiate

appropriate treatment and supportive measures.

Aluminum Toxicity
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 10% is administered, the patient's 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 intravenous administration with Intralipid 10%, perform liver tests to monitor for PNALD. If patients develop liver test abnormalities, consider discontinuation of Intralipid or dosage reduction. (See WARNINGS section)

Frequent platelet counts should be done in neonatal patients receiving parenteral nutrition with Intralipid 10%.

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: 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.

ADVERSE REACTIONS

The adverse reactions observed can be separated into two classes:
1. Those more frequently encountered are due: either to contamination of the intravenous catheter and result in sepsis, or to 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 10% (A 10% I.V. Fat Emulsion).
2. Less frequent reactions more directly related to Intralipid 10% 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, hypersensitivity reactions, including anaphylaxis (see CONTRAINDICATIONS, WARNINGS: Hypersensitivity 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 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 10%. The causes and significance of this phenomenon are unknown.

OVERDOSAGE

In the event of overdose, serious adverse reactions may result. Stop the infusion of Intralipid 10% 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 10% should be administered as a part of Intravenous nutrition via peripheral vein or by central venous infusion.

The recommended nutritional requirements of fat and recommended dosages of Intralipid to be administered to meet those requirements for adults and pediatric patients are provided below, along with recommendations for the initial and maximum infusion rates. Do not exceed the recommended maximum infusion rate.

Adult Patients

The initial rate of infusion in adults should be 1 mL/minute for the first 15 to 30 minutes of infusion. If no untoward reactions occur (see ADVERSE REACTIONS section), the infusion rate can be increased to 2 mL/minute. Not more than 500 mL of Intralipid 10% (A 10% I.V. Fat Emulsion) 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 of body weight (25 mL of Intralipid 10% per kg). Intralipid 10% should make up no more than 60% of the total caloric input to the patient. Maximum infusion rate should not exceed 0.1 g/kg/hr.

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 (5 mL Intralipid 10%) and may be increased in relation to the infant's ability to eliminate fat. The maximum recommended dosage is 3 g fat/kg/24 hours.

Pediatric patients may be at risk for parenteral nutrition-associated liver disease (PNALD), also known as intestinal failure-associated liver disease (see WARNINGS section) when receiving Intralipid for durations exceeding two weeks. During intravenous administration of Intralipid 10%, perform liver tests to monitor for PNALD.

The initial rate of infusion in older pediatric patients should be no more than 0.1

mL/minute for the first 10 to 15 minutes. If no untoward reactions occur, the rate can be changed to permit infusion of 1 mL of Intralipid 10%/kg/hour (equivalent to 0.1 g/kg/hour). The daily dosage should not exceed 3 g of fat/kg of body weight[3]. Intralipid 10% (equivalent to 0.125 g/kg/hour) 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 10% (A 10% I.V. Fat Emulsion) is administered to correct essential fatty acid deficiency, eight to ten percent of the caloric input should be supplied by Intralipid 10% in order to provide adequate amounts of linoleic and linolenic acids. When EFAD occurs together with stress, the amount of Intralipid 10% 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 10% 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. Use a 1.2 micron filter with Intralipid 10%. 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 10% extract DEHP from these PVC components and it may be advisable to consider infusion of Intralipid 10% through a non-DEHP administration set. 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 10% (A 10% 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).

Protect the admixed PN solution from light.

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 10% (A 10% Intravenous Fat Emulsion)

Note: Amino Acid Injection, Dextrose Injection and Intralipid 10% 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 10% and in no case should Intralipid 10% 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 10% is supplied as a sterile emulsion in the following fill sizes: 100 mL, 250 mL and 500 mL.

100 mL: 0338-0518-48
250 mL: 0338-0518-02
500 mL: 0338 0518-03

STORAGE

Intralipid 10% should not be stored above 25°C (77°F). Do not freeze Intralipid 10%. 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.

Revised: July 2025

Manufactured for
Baxter Healthcare Corporation
Deerfield, IL 60015 USA

Manufactured by:
Fresenius Kabi,
Uppsala, Sweden

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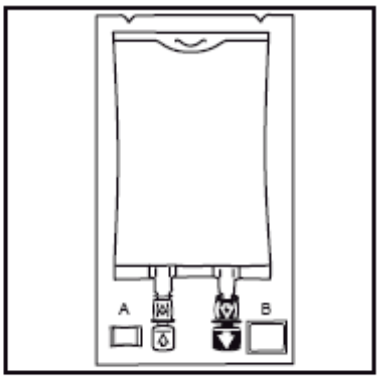
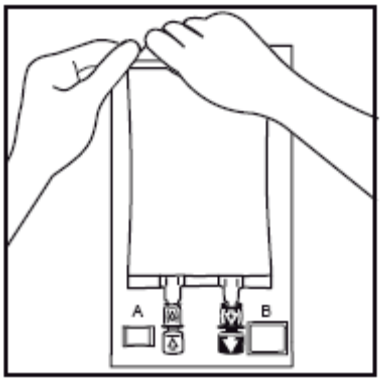
Instruction for Use - Intralipid® 10% Container

1.



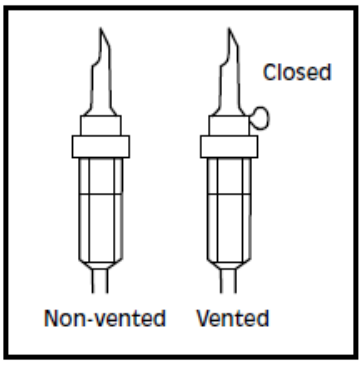
1. The integrity indicator (Oxalert™) A should be inspected before removing the overwrap. If the indicator is black the overwrap is damaged and the product should be discarded.

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 discarded. Place the bag on a clean, flat surface or hang on a support hook.

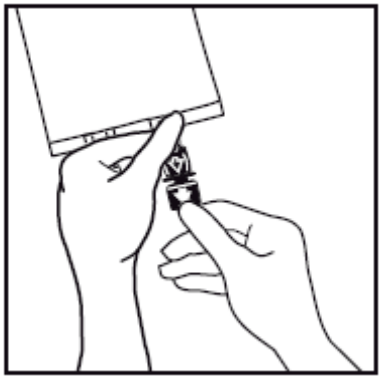
3.



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.

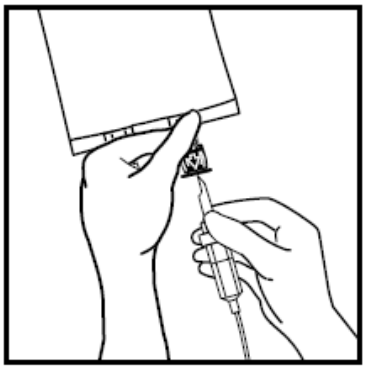
Use a 1.2 micron filter as part of the infusion set. Filters of less than 1.2 micron pore size must not be used.

4



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

5

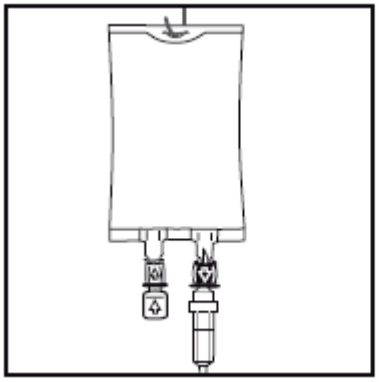


5. Hold the base of the infusion port firmly and insert the spike straight through the center of the septum by rotating the wrist slightly if needed.

NOTE: Assure that the spike is inserted straight into the port and not at an angle.

Inspect the bag and contents for particulate matter in a well-lit environment prior to administration. Discard the bag if there are any signs of discoloration or particulates.

6



6. Hang the bag in the hanger cut and start infusion.

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use INTRALIPID® safely and effectively. See full prescribing information for INTRALIPID.

INTRALIPID 20% (lipid injectable emulsion), for intravenous use
Initial U.S. Approval: 1975

---------- RECENT MAJOR CHANGES----------

Warnings and Precautions (5.3) 7/2025

----------INDICATIONS AND USAGE ----------

Intralipid is indicated as a source of calories and essential fatty acids for adult and pediatric patients requiring parenteral nutrition (PN) and as a source of essential fatty acids for prevention of essential fatty acid deficiency (EFAD).

----------DOSAGE AND ADMINISTRATION----------

- For intravenous infusion into a peripheral or central vein. (2.1)
- Intralipid Pharmacy Bulk Package is only indicated for use in pharmacy admixture program for the preparation of three-in-one or total nutrition admixtures (TNAs). (2.2)
- Protect the admixed PN solution from light. (2.2, 16)
- Recommended dosage depends on age, energy expenditure, clinical status, body weight, tolerance, ability to metabolize and eliminate lipids, and consideration of additional energy given to the patient. (2.3)

Age	Nutritional Requirements	
	Initial Recommended Dosage	Maximum Dosage
Birth to 2 years of age (including preterm and term neonates)	0.5 g/kg/day	3 g/kg/day
Pediatric patients 2 to <12 years of age	1 to 2 g/kg/day	2.5 g/kg/day
Pediatric patients 12 to 17 years of age	1 g/kg/day	2 g/kg/day
Adults	1 g/kg/day (stable) ≤1 g/kg/day (critically ill)	2.5 g/kg/day

----------DOSAGE FORMS AND STRENGTHS ----------

20% Injectable emulsion:

- 20 g/100 mL (0.2 g/mL) of lipid in 100 mL single-dose flexible container (3)
- 50 g/250 mL (0.2 g/mL) of lipid in 250 mL single-dose flexible container (3)
- 100 g/500 mL (0.2 g/mL) of lipid in 500 mL single-dose flexible container (3)
- 200 g/1,000 mL (0.2 g/mL) of lipid in 1,000 mL Pharmacy Bulk Package (3)

----------CONTRAINDICATIONS----------

- Known hypersensitivity to egg, soybean, or peanut, or any of the active ingredients or excipients. (4, 5.3)
- Severe disorders of lipid metabolism characterized by hypertriglyceridemia (serum triglyceride > 1,000 mg/dL). (4, 5.7)

----------WARNINGS AND PRECAUTIONS----------

- Risk of Clinical Decompensation with Rapid Infusion of Intravenous Lipid Emulsion in Neonates and Infants: Acute respiratory distress, metabolic acidosis, and death after rapid infusion of intravenous lipid emulsions have been reported. (5.1, 8.4)
- Risk of Parenteral Nutrition-Associated Liver Disease (PNALD): Increased risk in patients who receive PN for extended periods of time, especially preterm neonates. Monitor liver function tests; if abnormalities occur consider discontinuation or dosage reduction. (5.2, 6.1, 8.4)
- Hypersensitivity Reactions: Monitor for signs or symptoms. Discontinue infusion if reactions occur. (5.3)
- Risk of Infections, Fat Overload Syndrome, Refeeding Syndrome, and Hypertriglyceridemia: Monitor for signs and symptoms; monitor laboratory parameters. (5.4, 5.5, 5.6, 5.7)
- Aluminum Toxicity: Increased risk in patients with renal impairment, including preterm neonates. (5.8, 8.4)

----------ADVERSE REACTIONS----------

Most common adverse drug reactions (≥5%) from clinical trials in adults were nausea, vomiting, and pyrexia. Most common adverse drug reactions (≥5%) from clinical trials in pediatric patients were anemia, vomiting, increased gamma-glutamyltransferase, and cholestasis. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Fresenius Kabi at 1-800-551-7176 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

----------DRUG INTERACTIONS----------

Vitamin K Antagonists (e.g., warfarin): Anticoagulant activity may be counteracted; increase monitoring of coagulation parameters. (7)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 7/2025

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Intralipid® is indicated as a source of calories and essential fatty acids for adult and pediatric patients requiring parenteral nutrition (PN) and as a source of essential fatty acids for prevention of essential fatty acid deficiency (EFAD).

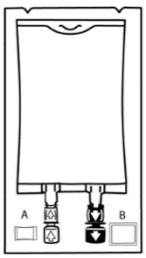
2 DOSAGE AND ADMINISTRATION

2.1 Important Administration Instructions

- Intralipid is prepared and administered by a healthcare provider in the inpatient setting. Patients and caregivers may prepare and administer Intralipid for home use after appropriate training by a trained healthcare provider.
- Intralipid is for intravenous infusion into a central or peripheral vein.
- Do not exceed the recommended maximum infusion rate in Table 1 *[see Dosage and Administration (2.3) and Warnings and Precautions (5.1)]*.
- Intralipid admixtures with osmolarity
  - Greater than or equal to 900 mOsm/L must be infused through a central vein.
  - Less than 900 mOsm/L may be administered either through a central or peripheral vein.
- Use a 1.2 micron in-line filter during administration.
- Use a dedicated infusion line without any connections. Do not connect multiple medications in series.
- To prevent air embolism, use a non-vented infusion set or close the vent on a vented set and fully evacuate residual gas in the bag prior to administration.
- Do not pressurize the flexible bag to increase flow rates, and if administration is controlled by a pumping device, turn off the pump before the bag runs dry.
- Do not use infusion sets and lines that contain di-2-ethylhexyl phthalate (DEHP), including infusion sets that contain polyvinyl chloride (PVC) components, because they contain DEHP as a plasticizer.
- Intralipid can be infused concurrently into the same vein as dextrose-amino acid solutions (as part of PN) by a Y-connector located near the infusion site; flow rates of each solution should be controlled separately by infusion pumps.
- After connecting the infusion set, start infusion of Intralipid immediately. Complete the infusion within 12 hours when using a Y-connector and within 24 hours when used as part of an admixture.

2.2 Preparation Instructions

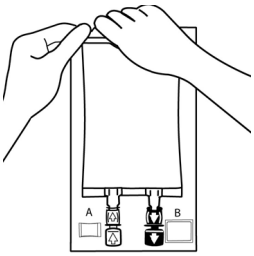
Use the following instructions to prepare single-dose 100 mL, 250 mL, and 500 mL Flexible containers for administration:



1. Inspect Bag
   - Inspect the integrity indicator (Oxalert®) (A) before removing the overpouch.
   - Discard the product if the indicator is black,

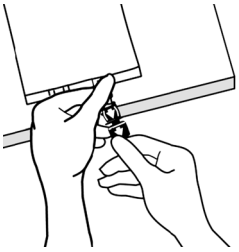
overpouch is opened or damaged, emulsion color is not white, or seals of bag are broken.

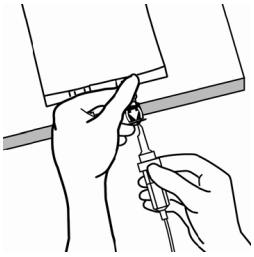
2. Remove Overpouch



- Place the bag on a clean, flat surface.
- Tear the overpouch at notch and pull down.
- Discard the Oxalert sachet (A) and the oxygen absorber (B).
- Visually inspect the bag and contents for particulate matter and discoloration prior to administration. The lipid emulsion should be a homogenous liquid with a milky white appearance. If the mixture is not white or the emulsion has separated (noted by discoloration, phase separation, or oily droplets), or if particulates and/or leakage are observed, discard the bag.

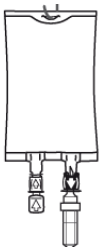
3. Spike Bag





- Identify the infusion port (**blue** cap with the arrow pointing away from the bag).
- Immediately before inserting the infusion set, break off the **blue** infusion port cap.
- Use infusion sets according to ISO Number 8536-4 with an external spike diameter of 5.5 to 5.7 mm and use a non-vented infusion set or close the air-inlet on a vented set.
- Use a 1.2 micron in-line filter for administration.
- Hold the base of the infusion port.
- Insert the spike through the infusion port by rotating your wrist slightly until the spike is inserted.
- Do not pierce the infusion port more than once.

4. Hang the bag



- On the hanger cut and start infusion.
- Discard unused portion.

<u>Intralipid 100 mL, 250 mL, and 500 mL single-dose Flexible Containers</u>

- After removing the overpouch, infuse immediately. If not used immediately, the product should be stored at 2°C to 8°C (36°F to 46°F) for no longer than 24 hours. After removal from storage, infuse within 12 hours when using a Y-connector and within 24 hours when used as part of an admixture.

Intralipid 1,000 mL Pharmacy Bulk Package

- *For admixing use only and not for direct intravenous infusion*. Prior to administration, transfer to a separate PN container for individual patient use.
- Transfer the contents through the blue infusion port using a suitable sterile transfer device or dispensing set. Discard any unused contents.
- Use the Pharmacy Bulk Package immediately for admixing after removal from the overpouch. If not used immediately, the product can be stored for no longer than 24 hours at 2°C to 8°C (36°F to 46°F). After removal from storage, and once the closure is penetrated, use Pharmacy Bulk Package contents within 4 hours.

Admixing Instructions

- Prepare the admixture in PN containers using strict aseptic techniques to avoid microbial contamination.
- Do not add Intralipid to the PN container first; destabilization of the lipid may occur. The prime destabilizers of emulsions are excessive acidity (such as a pH <5) and inappropriate electrolyte content. Amino acid solutions exert buffering effects that protect the emulsion from destabilization. Give careful consideration to the addition of divalent cations (Ca++ and Mg++), which have been shown to cause emulsion instability.
- Do not inject additives directly into Intralipid.
- Intralipid may be mixed with amino acid and dextrose injections to produce "all-in-one" PN admixtures. The mixing sequence below must be followed for manual compounding to minimize pH-related problems by ensuring that typically acidic dextrose injections are not mixed with lipid emulsions alone; shake bags gently after each addition.
    - Transfer dextrose injection to the PN container.
    - Transfer amino acid injection.
    - Transfer Intralipid.
- Simultaneous transfer of amino acid injection, dextrose injection, and Intralipid to the PN container is also permitted; follow automated compounding device instructions as indicated. Use gentle agitation during admixing to minimize localized concentration effects.
- Additions to the PN admixtures should be evaluated by a pharmacist for compatibility. Questions about compatibility may be directed to Fresenius Kabi.
- Inspect the admixture to ensure that precipitates have not formed during preparation of the admixture and the emulsion has not separated. Discard the admixture if any of the above are observed.
- Infuse admixtures containing Intralipid immediately. If not used immediately, store admixtures under refrigeration at 2°C to 8°C (36°F to 46°F) for no longer than 24 hours. Infusion must be complete within 24 hours after removal from refrigeration. Discard any remaining admixture.
- Protect the admixed PN solution from light.

2.3 Recommended Dosage and Administration

- The recommended nutritional requirements of lipid and recommended dosages of Intralipid to be administered to meet those requirements for adults and pediatric patients are provided in

Table 1, along with recommendations for the initial and maximum infusion rates.

- The dosing of Intralipid depends on the patient's individual energy requirements influenced by age, body weight, tolerance, clinical status, and the ability to metabolize and eliminate lipids.
- When determining dose, energy supplied by dextrose and amino acids from PN, as well as energy from oral or enteral nutrition, has to be taken into account. Energy and lipid provided from lipid-based medications should also be taken into account (e.g., propofol).
- Prior to administration of Intralipid, correct severe fluid and electrolyte disorders and measure serum triglyceride levels to establish a baseline value. In patients with elevated triglyceride levels, initiate Intralipid at a lower dosage and titrate in smaller increments, monitoring the triglyceride levels with each adjustment *[see Warnings and Precautions (5.7)]*.

Table 1: Recommended Pediatric and Adult Dosage and Infusion Rate

Age	Nutritional Requirements	Direct Infusion Rate	
	Recommended Initial Dosage and Maximum Dosage	Initial	Maximum
Birth to 2 years of age (including preterm and term neonates*) *[see Warnings and Precautions (5.1)]*	Initial 0.5 g/kg/day not to exceed 3 g/kg/day**	0.1 mL/kg/hour for the first 10 to 15 minutes; gradually increase to the required rate after 15 minutes	0.75 mL/kg/hour
Pediatric patients 2 to <12 years of age	Initial 1 to 2 g/kg/day not to exceed 2.5 g/kg/day***	0.2 to 0.4 mL/kg/hour for the first 10 to 15 minutes; gradually increase to the required rate after 15 minutes	0.75 mL/kg/hour
Pediatric patients 12 to 17 years of age	Initial 1 g/kg/day not to exceed 2 g/kg/day**	0.2 mL/kg/hour for the first 10 to 15 minutes; gradually increase to the required rate after 15 minutes	0.75 mL/kg/hour
Adults	1 g/kg/day in stable patients ≤1 g/kg/day in critically ill patients not to exceed 2.5 g/kg/day; not more than 500 mL of Intralipid should be infused on the first day of therapy**	0.2 mL/kg/hour for the first 10 to 15 minutes; gradually increase to the required rate after 30 minutes	0.5 mL/kg/hour

* The neonatal period is defined as including term, post-term, and preterm neonates. The neonatal period for term and post-term neonates is the day of birth plus 27 days. For preterm neonates, the neonatal period is defined as the day of birth through the expected age of delivery plus 27 days (i.e., 44 weeks post-menstrual age).

** Daily dosage should also not exceed a maximum of 60% of total energy requirements *[see Overdosage (10)]*.

Dosage Modifications in Patients with Essential Fatty Acid Deficiency

When Intralipid is administered to correct essential fatty acid deficiency (EFAD), supply 8% to 10% of caloric input from Intralipid in order to provide adequate amounts of linoleic and linolenic acids.

3 DOSAGE FORMS AND STRENGTHS

Intralipid 20% is a sterile, homogenous, milky, white lipid injectable emulsion in Flexible Containers supplied as:

- 20 g/100 mL (0.2 g/mL) of lipid in 100 mL single-dose Flexible Container
- 50 g /250 mL (0.2 g/mL) of lipid in 250 mL single-dose Flexible Container
- 100 g/500 mL (0.2 g/mL) of lipid in 500 mL single-dose Flexible Container
- 200 g /1,000 mL (0.2 g/mL) of lipid in 1,000 mL Pharmacy Bulk Package

4 CONTRAINDICATIONS

- Known hypersensitivity to egg, soybean, peanut, or any of the active or inactive ingredients in Intralipid *[see Warnings and Precautions (5.3)]*
- Severe disorders of lipid metabolism characterized by hypertriglyceridemia (serum triglyceride > 1,000 mg/dL) *[see Warnings and Precautions (5.7)]*

5 WARNINGS AND PRECAUTIONS

5.1 Clinical Decompensation with Rapid Infusion of Intravenous Lipid Emulsions in Neonates and Infants

In the postmarketing setting, serious adverse reactions including acute respiratory distress, metabolic acidosis, and death have been reported in neonates and infants after rapid infusion of intravenous lipid emulsions. Hypertriglyceridemia was commonly reported.

Strictly adhere to the recommended total daily dosage; the hourly infusion rate should not exceed 0.75 mL/kg/hour *[see Dosage and Administration (2.3)]*.

Preterm and small for gestational age infants have poor clearance of intravenous lipid emulsion and increased free fatty acid plasma levels following lipid emulsion infusion.

Carefully monitor the infant's ability to eliminate the infused lipids from the circulation (e.g., measure serum triglycerides and/or plasma free fatty acid levels). If signs or poor clearance of lipids from the circulation occur, stop the infusion and initiate a medical evaluation *[see Warnings and Precautions (5.5, 5.7) and Overdosage (10)]*.

5.2 Parenteral Nutrition-Associated Liver Disease and Other Hepatobiliary Disorders

Risk of Parenteral Nutrition-Associated Liver Disease

Parenteral nutrition-associated liver disease (PNALD), also referred to as intestinal failure-associated liver disease (IFALD), can present as cholestasis or hepatic steatosis, and may

progress to steatohepatitis with fibrosis and cirrhosis (possibly leading to chronic hepatic failure). The etiology of PNALD is multifactorial; however, intravenously administered phytosterols (plant sterols) contained in plant-derived lipid emulsions, including Intralipid, have been associated with development of PNALD.

In a randomized study of neonates and infants expected to be treated with PN for at least 28 days, parenteral nutrition-associated cholestasis (PNAC), a precursor to PNALD, developed more frequently in Intralipid-treated patients than patients treated with a 4-oil mixed lipid emulsion. *[see Adverse Reactions (6.1), Use in Specific Populations (8.4)]*.

Monitor liver tests in patients treated with Intralipid and consider discontinuation or dosage reduction if abnormalities occur.

Other Hepatobiliary Disorders
Hepatobiliary disorders including cholecystitis and cholelithiasis have developed in some PN-treated patients without preexisting liver disease.

Monitor liver tests when administering Intralipid. Patients developing signs of hepatobiliary disorders should be assessed early to determine whether these conditions are related to Intralipid use.

5.3 Hypersensitivity Reactions

Intralipid contains soybean oil and egg phospholipids, which may cause hypersensitivity reactions. Cross reactions have been observed between soybean and peanut. In postmarketing experience, anaphylaxis has been reported following Intralipid administration *[see Adverse Reactions (6.2)]*.

Intralipid is contraindicated in patients with known hypersensitivity to egg, soybean, peanut or any of the active or inactive ingredients in Intralipid *[see Contraindications (4)]*. If a hypersensitivity reaction occurs, stop infusion of Intralipid immediately and initiate appropriate treatment and supportive measures.

5.4 Infections

Parenteral nutrition, such as Intralipid, can support microbial growth and is an independent risk factor for the development of catheter-related bloodstream infections. To decrease the risk of infectious complications, ensure aseptic techniques are used for catheter placement, catheter maintenance, and preparation and administration of Intralipid.

Monitor for signs and symptoms of infection including fever and chills, as well as laboratory test results that might indicate infection (including leukocytosis and hyperglycemia). Perform frequent checks of the intravenous catheter insertion site for edema, redness, and discharge.

5.5 Fat Overload Syndrome

Fat overload syndrome is a rare condition that has been reported with intravenous lipid injectable emulsions and is characterized by a sudden deterioration in the patient's condition (e.g., fever,

anemia, leukopenia, thrombocytopenia, coagulation disorders, hyperlipidemia, hepatomegaly, deteriorating liver function, and central nervous system manifestations such as coma). A reduced or limited ability to metabolize lipids, accompanied by prolonged plasma clearance (resulting in higher lipid levels), may result in this syndrome. Although fat overload syndrome has been most frequently observed when the recommended lipid dose or infusion rate was exceeded, cases have also been described when the lipid formulation was administered according to instructions.

If signs or symptoms of fat overload syndrome occur, stop the infusion of Intralipid. The syndrome is usually reversible when the infusion of the lipid emulsion is stopped.

5.6 Refeeding Syndrome

Administering PN to severely malnourished patients may result in refeeding syndrome, which is characterized by the intracellular shift of potassium, phosphorus, and magnesium as patients become anabolic. Thiamine deficiency and fluid retention may also develop. To prevent these complications, closely monitor severely malnourished patients and slowly increase their nutrient intake.

5.7 Hypertriglyceridemia

The use of Intralipid is contraindicated in patients with hypertriglyceridemia with serum triglyceride concentrations >1,000 mg/dL.

Patients with conditions such as inherited lipid disorders, obesity, diabetes mellitus, or metabolic syndromes have a higher risk of developing hypertriglyceridemia with the use of Intralipid. In addition, patients with hypertriglyceridemia may have worsening of their hypertriglyceridemia with administration of Intralipid. Excessive dextrose administration may further increase such risk.

Evaluate patients' capacity to metabolize and eliminate the infused lipid emulsion by measuring serum triglycerides before the start of infusion (baseline value) and regularly throughout treatment. If triglyceride levels are above 400 mg/dL in adults, stop the Intralipid infusion and monitor serum triglyceride levels to avoid clinical consequences of hypertriglyceridemia such as pancreatitis. In pediatric patients with hypertriglyceridemia, lower triglyceride levels (i.e., below 400 mg/dL) may be associated with adverse reactions. Monitor serum triglyceride levels to avoid potential complications with hypertriglyceridemia such as pancreatitis, lipid pneumonitis, and neurologic changes, including kernicterus.

To minimize the risk of new or worsening of hypertriglyceridemia, assess high-risk patients for their overall energy intake including other sources of lipids and dextrose, as well as concomitant drugs that may affect lipid and dextrose metabolism.

5.8 Aluminum Toxicity

Intralipid contains no more than 25 mcg/L of aluminum. Prolonged PN administration in patients with renal impairment may result in aluminum reaching toxic levels. Preterm neonates are at greater risk because their kidneys are immature, and they require large amounts of calcium and phosphate solutions that contain aluminum.

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

5.9 Monitoring/Laboratory Tests

Monitor fluid status closely in patients with pulmonary edema or heart failure.

Throughout treatment, monitor serum triglycerides *[see Warnings and Precautions (5.7)],* essential fatty acids, fluid and electrolyte status, serum osmolarity, blood glucose, liver and kidney function, blood count (including platelets), and coagulation parameters.

The lipids contained in Intralipid may interfere with some laboratory tests (e.g., hemoglobin, lactate dehydrogenase, bilirubin, oxygen saturation) if blood is sampled before lipids have cleared from the bloodstream. Conduct these tests at least 6 hours after stopping the infusion.

Intralipid contains vitamin K that may counteract anticoagulant activity *[see Drug Interactions (7)]*.

6 ADVERSE REACTIONS

Adverse reactions described elsewhere in this Prescribing Information are:

- Clinical Decompensation with Rapid Infusion of Intravenous Lipid Emulsion in Neonates and Infants *[see Warnings and Precautions (5.1)]*
- Parenteral Nutrition-Associated Liver Disease and Other Hepatobiliary Disorders *[see Warnings and Precautions (5.2)]*
- Hypersensitivity Reactions *[see Warnings and Precautions (5.3)]*
- Infections *[see Warnings and Precautions (5.4)]*
- Fat Overload Syndrome *[see Warnings and Precautions (5.5)]*
- Refeeding Syndrome *[see Warnings and Precautions (5.6)]*
- Hypertriglyceridemia *[see Warnings and Precautions (5.7)]*
- Aluminum Toxicity *[see Warnings and Precautions (5.8)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

Intralipid or equivalent soybean oil lipid emulsions functioned as the comparator in trials of the 4-oil mixed lipid emulsion *[see Clinical Studies (14)]*. The adverse reactions from these studies are included to present the clinical experience with Intralipid.

The safety database for Intralipid or equivalent soybean oil lipid emulsion exposure in these studies includes 393 patients (230 adults; 163 pediatric) in 9 clinical trials. Adult patients were exposed for 5 days to 4 weeks in 5 clinical trials. Intralipid or equivalent soybean oil lipid

emulsion was used as a component of PN which also included dextrose, amino acids, vitamins, and trace elements. Two of the 5 studies in adults were performed with Intralipid as a component of PN delivered in a 3-chamber bag.

Table 2: Adverse Reactions in >1% of Adult Patients Treated with Intralipid/Soybean oil emulsion

Adverse Reaction	Number of Patients in Soybean Oil Lipid Emulsion Group (N=230)	Number of Patients in 4-Oil Mixed Lipid Emulsion Comparator Group (N=229)
Nausea	26 (11%)	20 (9%)
Vomiting	12 (5%)	15 (7%)
Pyrexia	11 (5%)	9 (4%)
Hypertension	9 (4%)	6 (3%)
Headache	7 (3%)	3 (1%)
Hyperglycemia	5 (2%)	12 (5%)
Abdominal pain	5 (2%)	8 (4%)
Flatulence	4 (2%)	10 (4%)
Blood triglycerides increased	4 (2%)	6 (3%)
Sepsis	4 (2%)	5 (2%)
Diarrhea	4 (2%)	3 (1%)
Pneumonia	4 (2%)	3 (1%)
Pruritus	4 (2%)	3 (1%)
Gamma-glutamyltransferase increased	4 (2%)	2 (1%)

Less common adverse reactions occurring in ≤1% of adult patients who received Intralipid or equivalent soybean oil lipid emulsion were dyspepsia, urinary tract infection, anemia, infection, dyspnea, cholestasis, dysgeusia, increased blood alkaline phosphatase, tachycardia, liver function test abnormalities, dizziness, rash, and thrombophlebitis.

The 163 patients treated with Intralipid in four pediatric trials consisted of 147 patients <28 days of age, 9 patients 28 days to <2 years of age, and 7 patients 2 to 7 years of age; the duration of exposure was 7 to 84 days. Fifty-six percent of the pediatric patients were female, and 85% were Caucasian. Most pediatric patients were preterm neonates with feeding intolerance or other conditions requiring short-term (<29 days) PN.

Table 3: Adverse Reactions in >1% of Pediatric Patients Treated with Intralipid

Adverse Reaction	Number of Patients in Intralipid Group (N=163)	Number of Patients in 4-Oil Mixed Lipid Emulsion Comparator Group (N=170)
Anemia	33 (20%)	30 (18%)
Vomiting	16 (10%)	16 (9%)
Gamma-glutamyltransferase increased	12 (7%)	10 (6%)
Cholestasis	10 (6%)	7 (4%)
Pyrexia	7 (4%)	7 (4%)
C-reactive protein increased	7 (4%)	6 (4%)
Hyperbilirubinemia	7 (4%)	5 (3%)
Bilirubin conjugated increased	7 (4%)	3 (2%)
Nosocomial infection	6 (4%)	10 (6%)
Blood alkaline phosphatase increased	6 (4%)	1 (1%)
Abdominal pain	5 (3%)	4 (2%)
Hematocrit decreased	5 (3%)	2 (1%)
Metabolic acidosis	5 (3%)	2 (1%)
Diarrhea	4 (3%)	3 (2%)
Tachycardia	4 (3%)	3 (2%)
Thrombocytopenia	4 (3%)	3 (2%)
Alanine aminotransferase increased	3 (2%)	1 (1%)
Aspartate aminotransferase increased	3 (2%)	0 (0%)
Parenteral nutrition-associated liver disease	3 (2%)	0 (0%)

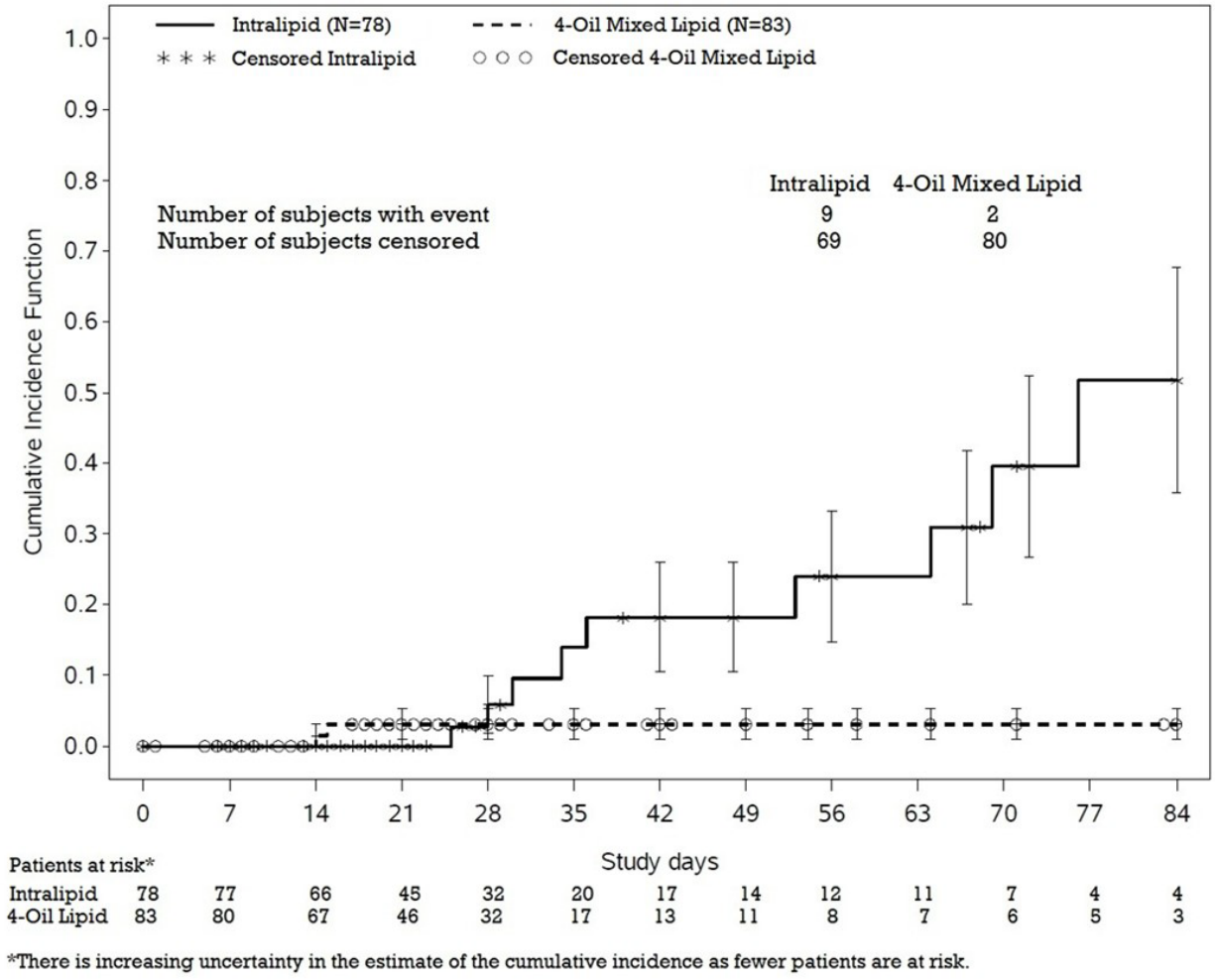
Less common adverse reactions occurring in ≤1% of pediatric patients who received Intralipid were hyperglycemia, sepsis, increased blood triglycerides, infection, fluid overload, hypertension, hypertriglyceridemia, rash, and hyperlipidemia.

In a randomized active-controlled, double-blind, parallel-group, multi-center study that included 152 neonates and 9 patients ranging in age from 29 to 153 days who were expected to require PN for at least 28 days, PNAC, a precursor to PNALD, developed more frequently in Intralipid-treated patients than in patients treated with a comparator 4-oil mixed lipid emulsion.

PNAC (defined as direct bilirubin >2 mg/dL with a second confirmed elevation >2 mg/dL at least 7 days later) occurred in 11.5% (9/78) in Intralipid-treated patients and 2.4% (2/83) of patients treated with a 4-oil mixed lipid emulsion. Most PNAC events occurred in patients who were treated for longer than 28 days.

The estimated cumulative incidence of PNAC is shown in the Kaplan-Meier cumulative incidence curve in Figure 1 *[see Pediatric Clinical Studies (14.2)]*.

Figure 1: Cumulative Incidence Curve of Time to Parenteral Nutrition-Associated Cholestasis (PNAC) with Standard Error Bars



*There is increasing uncertainty in the estimate of the cumulative incidence as fewer patients are at risk.

6.2 Postmarketing Experience

The following adverse reactions from voluntary reports have been reported with Intralipid. Because many of these reactions were reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Cardiac disorders: palpitations
Gastrointestinal disorders: vomiting, nausea
General disorders and administration site conditions: chills, chest discomfort, pyrexia
Nervous system disorders: dizziness
Respiratory, thoracic, and mediastinal disorders: dyspnea
Immune system disorders: hypersensitivity reactions, including anaphylaxis *[see Contraindications (4), Warnings and Precautions (5.3)]*
Vascular disorders: phlebitis

Blood and lymphatic system disorders: hypercoagulability

7 DRUG INTERACTIONS

Soybean oil in Intralipid contains vitamin K_1 which may counteract the anticoagulant activity of vitamin K antagonists such as warfarin. In patients who receive concomitant Intralipid and warfarin, increase monitoring of laboratory parameters for anticoagulant activity.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Administration of the recommended dose of Intralipid is not expected to cause major birth defects, miscarriage, or other adverse maternal or fetal outcomes. No animal reproduction studies have been conducted with Intralipid. There are risks to the fetus associated with severe malnutrition during pregnancy *(see Clinical Considerations)*.

The background risk of major birth defects and miscarriage for the indicated population(s) is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Clinical Considerations

Disease-Associated Maternal and/or Embryo-Fetal Risk

Severe malnutrition in pregnant women is associated with preterm delivery, low birth weight, intrauterine growth restriction, congenital malformations, and perinatal mortality. Parenteral nutrition should be considered if the pregnant woman's nutritional requirements cannot be fulfilled by oral or enteral intake.

8.2 Lactation

Risk Summary

Administration of the recommended dose of Intralipid is not expected to cause harm to a breastfed infant. There are no data on the presence of Intralipid in human or animal milk or its effects on milk production. Available published literature includes fewer than five reported cases of breastfed infants exposed to various lipid emulsions via lactation, and these cases did not report adverse events. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Intralipid and any potential adverse effects of Intralipid on the breastfed infant, or from the underlying maternal condition.

8.4 Pediatric Use

Intralipid is contraindicated in pediatric patients with severe disorders of lipid metabolism [*(see Contraindications (4)]*.

The safety and effectiveness of Intralipid have been established as a source of calories and essential fatty acids for PN in pediatric patients, including term and preterm neonates. Use of

Intralipid in neonates is supported by evidence from short-term (i.e., 1- to 4- week) studies, and one study following neonates beyond 4 weeks *[see Clinical Studies (14.2)]*. Use of Intralipid in older pediatric patients is supported by evidence from short-term (i.e., <28 days) studies in pediatric patients 28 days to 12 years of age and additional evidence from studies in adults *[see Clinical Studies (14)]*. The most common adverse reactions in Intralipid-treated pediatric patients were anemia, vomiting, gamma-glutamyltransferase increased, and cholestasis. PNAC, a precursor to PNALD, developed more frequently in Intralipid-treated patients than in patients treated with a comparator 4-oil mixed lipid emulsion *[see Warnings and Precautions (5.1) and Adverse Reactions (6.1)]*.

In the postmarketing setting, clinical decompensation with rapid infusion of intravenous lipid emulsion in neonates and infants, sometimes fatal, has been reported *[see Warnings and Precautions (5.1)]*. Because of immature renal function, preterm neonates receiving prolonged treatment with Intralipid may be at risk for aluminum toxicity *[see Warnings and Precautions (5.8)]*.

8.5 Geriatric Use

Reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or drug therapy.

10 OVERDOSAGE

In the event of an overdose, serious adverse reactions may result *[see Warnings and Precautions (5.1, 5.5)]*. Stop the infusion of Intralipid until triglyceride levels have normalized and symptoms have abated. The effects are usually reversible by stopping the lipid infusion. If medically appropriate, further intervention may be indicated. Lipids are not dialyzable from plasma.

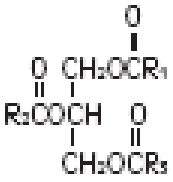
11 DESCRIPTION

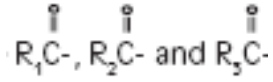
Intralipid is a sterile, non-pyrogenic, white, homogenous lipid emulsion for intravenous infusion as a source of calories and essential fatty acids. The lipid content of Intralipid is 0.2 g/mL and comprises soybean oil. The phosphate content is 15 mmol/L.

The total energy content, including fat, phospholipids, and glycerin is 2,000 kcal/L.

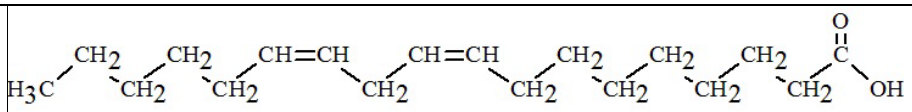
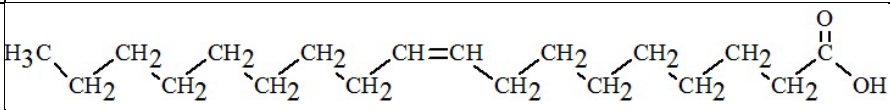
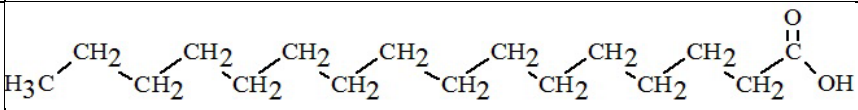
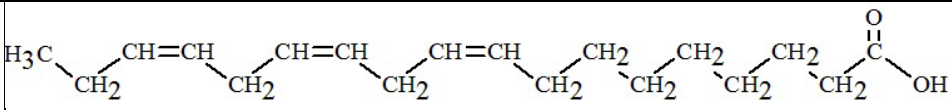
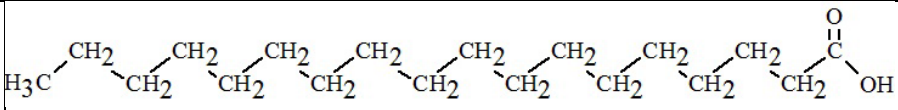
Each 100 mL of Intralipid contains approximately 20 g soybean oil, 1.2 g egg yolk phospholipids, 2.25 g glycerin, water for injection, and sodium hydroxide for pH adjustment (pH 6 to 8.9). Intralipid has an osmolality of approximately 350 mOsmol/kg water (which represents an osmolarity of 260 mOsmoL/L).

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

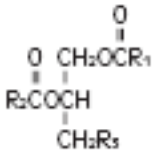


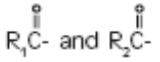
where  are saturated and unsaturated fatty acid residues.

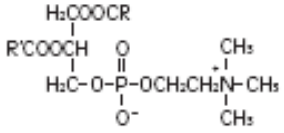
The major component fatty acids in Intralipid are linoleic acid (44% to 62%), oleic acid (19% to 30%), palmitic acid (7% to 14%), alpha-linolenic acid (4% to 11%), and stearic acid (1.4% to 5.5%). These fatty acids have the following chemical and structural formulas:

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 $C_{18}H_{36}O_2$	

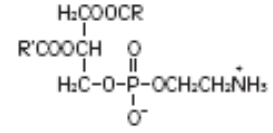
Purified egg phosphatides are a mixture of naturally occurring phospholipids which are isolated from the egg yolk. These phospholipids have the following general structure:



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

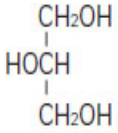


Phosphatidylcholine



Phosphatidylethanolamine

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



The container-solution 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 oxygen and moisture barrier when necessary.

Intralipid contains no more than 25 mcg/L of aluminum.

The container is not made with natural rubber latex, PVC, or DEHP.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Intralipid provides a biologically utilizable source of calories and essential fatty acids.

Fatty acids serve as an important substrate for energy production. The most common mechanism of action for energy production derived from fatty acid metabolism is beta oxidation. Fatty acids are also important for membrane structure and function, as precursors for bioactive molecules (such as prostaglandins), and as regulators of gene expression.

12.2 Pharmacodynamics

The pharmacodynamic effects of Intralipid have not been fully characterized.

12.3 Pharmacokinetics

Intralipid provides fatty acids in the form of triglycerides which are hydrolyzed by lipoprotein lipase to release free fatty acids. Linoleic acid and alpha-linolenic acid are metabolized within a common biochemical pathway through a series of desaturation and elongation steps.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity, genetic toxicology, and animal fertility studies have not been performed with Intralipid.

14 CLINICAL STUDIES

Intralipid or equivalent soybean oil lipid emulsion functioned as the comparator for the 4-oil mixed lipid emulsion in the clinical studies described in sections 14.1 and 14.2. The trial results are included to present the clinical experience with Intralipid.

14.1 Adult Clinical Studies

The efficacy of Intralipid or equivalent soybean oil lipid emulsion compared to a 4-oil mixed lipid emulsion was evaluated in 3 clinical studies in adult patients. Nutritional efficacy in adult studies was assessed by changes in anthropometric indices (body weight, height, and body mass index [BMI]), changes in lipid and protein metabolism (albumin), and fatty acid parameters. Of the 354 adult patients (178 Intralipid; 176 comparator), 62% were male, 99% were Caucasian, and ages ranged from 19 to 96 years. All patients received Intralipid/equivalent soybean oil lipid emulsion or the comparator as part of a PN regimen. Although Adult Study 1, Adult Study 2, and Adult Study 3 were not designed for formal statistical comparisons between Intralipid/equivalent soybean oil lipid emulsion and the comparator, they support Intralipid as a source of calories and essential fatty acids in adults. The lipid dosage was variable in these studies and adjusted to the patient's nutritional requirements.

Adult Study 1 was a double-blind, randomized, active-controlled, parallel-group, multicenter study in patients who required PN for at least 28 days. Seventy-five patients were enrolled, and 73 patients were treated with either Intralipid or the comparator. Changes in mean triglyceride levels from baseline values to Week 4 were similar in both the Intralipid and comparator groups. Mean albumin levels demonstrated a comparable decrease in both groups. Mean changes in body weight (kg) and BMI (kg/m2) were similar in both the Intralipid and the comparator groups.

Adult Study 2 was a phase 3, randomized, double-blind, active-controlled, multicenter study. A total of 249 postoperative adult patients were randomized to receive either an equivalent soybean oil lipid emulsion to Intralipid or the comparator for at least 5 days as part of their total parenteral nutrition (TPN) regimen. From baseline to Day 6, mean triglyceride levels increased similarly in both the soybean oil lipid emulsion and the comparator groups.

Adult Study 3 was a double-blind randomized, active-controlled, parallel-group, single-center study in 32 adult patients who required TPN for 10 to 14 days. Patients were treated with either an equivalent soybean oil lipid emulsion to Intralipid or the comparator. The increase in mean triglyceride levels from baseline to the final assessment was similar in both the soybean oil lipid emulsion and the comparator groups.

14.2 Pediatric Clinical Studies

The efficacy of Intralipid compared to a 4-oil mixed lipid emulsion in pediatric patients of all age groups, including term and preterm neonates, was evaluated in 333 patients in 4 randomized active-controlled, double-blind, parallel-group controlled clinical studies. Although Pediatric Studies 1, 2, 3, and 4 were not designed for formal statistical comparisons between Intralipid and the comparator, they support Intralipid as a source of calories and essential fatty acids in pediatric patients. The 333 pediatric patients (163 Intralipid; 170 comparator) consisted of 296 patients who were <28 days old, 22 patients 29 days to <2 years old, and 15 patients 2 to <12 years old. Fifty percent of the pediatric patients were male and 87% were Caucasian. All patients received Intralipid or the comparator as part of a PN regimen. Nutritional efficacy in neonates was assessed by changes in anthropometric indices (body weight, height, head circumference). Nutritional efficacy in pediatric patients, 28 days to 12 years of age, was assessed by changes in triglyceride concentrations and fatty acid parameters.

Pediatric Study 1 enrolled 152 preterm and term neonates (birth up to 28 days) and 9 patients ranging in age from 29 to 153 days. Patients were treated with either Intralipid (n=78) or the comparator (n=83). A total of 119 patients (58 Intralipid; 61 comparator) received study treatment for ≥14 days. A total of 27 patients received Intralipid for ≥29 days; 5 patients received Intralipid for the maximum study duration of 78-84 days.

Pediatric Studies 2 and 3 enrolled 60 and 84 preterm neonates, respectively, who were treated with either Intralipid or the comparator (72 neonates in each group). The median treatment duration for Intralipid group was 9 days in Pediatric Study 2 and 6 days in Pediatric Study 3.

Pediatric Study 4 enrolled 13 patients 5 months to <2 years of age and 15 patients 2 to 11.5 years of age. Patients were treated with either Intralipid (n=13) or the comparator (n=15) with a median treatment duration of 27 days.

In Pediatric Studies 1, 2 and 3, which enrolled neonates, Intralipid-treated patients showed increases in the median body weight, height/length, and head circumference (which was measured in Studies 1 and 3) comparable to the comparator-treated patients. Mean triglyceride levels from baseline to the final assessment in Pediatric Studies 1, 2, and 3 were variable in these neonates, but overall differences between groups were not considered clinically relevant. Mean triglyceride levels in Pediatric Study 4 were variable but remained within the normal range.

16 HOW SUPPLIED/STORAGE AND HANDLING

Intralipid 20% (lipid injectable emulsion, USP) is a sterile, homogeneous, milky, white lipid emulsion supplied in Flexible Containers as follows:

Product Code	**Unit of Use**	**Unit of Sale**
831800311	NDC 65219-531-01 One 100 mL **free***flex*® bag	NDC 65219-531-10 Package of 10 **free***flex*® bags
831818311	NDC 65219-533-01 One 250 mL	NDC 65219-533-25 Package of 10

	free*flex*® bag	**free***flex*® bags
831826311	NDC 65219-535-01 One 500 mL **free***flex*® bag	NDC 65219-535-50 Package of 12 **free***flex*® bags
831842311	NDC 65219-539-01 One 1,000 mL Pharmacy Bulk Package **free***flex*® bag	NDC 65219-539-10 Package of 6 **free***flex*® bags

Store below 25°C (77°F). Avoid excessive heat. Do not freeze. If accidentally frozen, discard container. Store in the overpouch until ready for use.

Intralipid 100 mL, 250 mL and 500 mL single-dose Flexible Containers

After removing the overpouch, infuse immediately. If not used immediately, the product should be stored at 2°C to 8°C (36°F to 46°F) for no longer than 24 hours. After removal from storage, infuse within 12 hours when using a Y-connector or within 24 hours if used as part of an admixture *[see Dosage and Administration (2.2)]*.

Intralipid 1,000 mL Pharmacy Bulk Package

Use the Pharmacy Bulk Package immediately for admixing after removal from the overpouch. If not used immediately, the product should be stored for no longer than 24 hours at 2°C to 8°C (36°F to 46°F). After removal from storage, and once the closure is penetrated, use Pharmacy Bulk Package contents within 4 hours *[see Dosage and Administration (2.2)]*.

Admixtures

Infuse admixtures containing Intralipid immediately. If not used immediately, admixtures should be stored at 2°C to 8°C (36°F to 46°F) for no longer than 24 hours. After removal from storage, infuse within 24 hours *[see Dosage and Administration (2.2)]*.

Protect the admixed PN solution from light *[see Dosage and Administration (2.2)]*.

17 PATIENT COUNSELING INFORMATION

When initiating Intralipid administration, discuss the following information with the patient or caregiver:

Clinical Decompensation with Rapid Infusion of Intravenous Lipid Emulsion in Neonates and Infants

Inform caregivers that acute respiratory distress and death may occur in neonates and infants after rapid infusion of intravenous lipid emulsions. If Intralipid is infused at home, instruct caregivers not to exceed the maximum infusion rate *[see Warnings and Precautions (5.1)]*.

Parenteral Nutrition-Associated Liver Disease and Other Hepatobiliary Disorders

Inform patients and caregivers that use of parenteral nutrition may result in parenteral nutrition-associated liver disease and/or other hepatobiliary disorders *[see Warnings and Precautions (5.2)]*.

Hypersensitivity Reactions

Inform patients and caregivers that Intralipid may cause hypersensitivity reactions, including anaphylaxis. If Intralipid is infused at home, instruct patients or caregivers to stop the infusion of Intralipid immediately and seek medical attention if they experience signs or symptoms of a hypersensitivity reaction, such as rapid or weak heartbeat, feeling faint, difficulty in breathing or swallowing, vomiting, nausea, headache, sweating, dizziness, hives, rash, itching, flushing, dizziness, fever, or chills *[see Warnings and Precautions (5.3)]*.

Infections

Inform patients and caregivers that patients who receive Intralipid are at risk of infection. If Intralipid is infused at home, instruct patients or caregivers to ensure aseptic techniques are used for the preparation and administration of Intralipid and to monitor for signs and symptoms of infection *[see Warnings and Precautions (5.4)]*.

Fat Overload Syndrome

Inform patients and caregivers that fat overload syndrome has been reported with the use of intravenous lipid emulsions. If Intralipid is infused at home, instruct patients or caregivers to stop the infusion of Intralipid if signs or symptoms of fat overload syndrome occur *[see Warnings and Precautions (5.5)]*.

Refeeding Syndrome

If the patient is severely malnourished, inform patients and caregivers that administering parenteral nutrition including Intralipid may result in refeeding syndrome *[see Warnings and Precautions (5.6)]*.

Hypertriglyceridemia

Inform patients and their caregivers about the risks of hypertriglyceridemia with Intralipid use *[see Warnings and Precautions (5.7)]*.

Aluminum Toxicity

Inform patients and their caregivers that prolonged PN administration in patients with renal impairment, including preterm neonates, may result in aluminum reaching toxic levels associated with central nervous system and bone toxicity *[see Warnings and Precautions (5.8)]*.

Preparation and Administration Instructions

If it is acceptable for a patient or caregiver to administer Intralipid at home, then provide recommendations on how to inspect and prepare, add compatible additives (when appropriate), administer, and store Intralipid *[see Dosage and Administration (2.1, 2.2)]*. Inform patients or caregivers not to deviate from the administration instructions given by the healthcare provider.

Manufactured by:

Uppsala, Sweden

Package Insert Part Number Pending

Intralipid® is a registered trademark of Fresenius Kabi AB.

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use INTRALIPID® safely and effectively. See full prescribing information for INTRALIPID.

INTRALIPID 30% (lipid injectable emulsion), for intravenous use
Initial U.S. Approval: 1993

---------- RECENT MAJOR CHANGES----------
Warnings and Precautions (5.3) 7/2025

----------INDICATIONS AND USAGE ----------
Intralipid is indicated as a source of calories and essential fatty acids for adult and pediatric patients requiring parenteral nutrition (PN) and as a source of essential fatty acids for prevention of essential fatty acid deficiency (EFAD).

----------DOSAGE AND ADMINISTRATION----------
- Intralipid 30% Pharmacy Bulk Package is for admixing only and is **not** intended for direct intravenous infusion. (2.1)
- Admixtures containing Intralipid 30% are prepared by a healthcare provider. (2.1)
- Intralipid 30% must be combined with other PN fluids so that the resulting admixture has a final lipid concentration of no more than 20% (0.2 g lipid per mL of admixture). (2.1, 2.2)
- Protect the admixed PN solution from light. (2.2, 16)
- Recommended dosage depends on age, energy expenditure, clinical status, body weight, tolerance, ability to metabolize and eliminate lipids, and consideration of additional energy given to the patient. (2.3)

Age	Nutritional Requirements
	Recommended Initial Dosage and Maximum Dosage
Birth to 2 years of age (including preterm and term neonates)	Initial 0.5 g/kg/day not to exceed 3 g/kg/day
Pediatric patients 2 to <12 years of age	Initial 1 to 2 g/kg/day not to exceed 2.5 g/kg/day
Pediatric patients 12 to 17 years of age	Initial 1 g/kg/day not to exceed 2 g/kg/day
Adults	1 g/kg/day (stable) ≤1 g/kg/day (critically ill) not to exceed 2.5 g/kg/day

---------- DOSAGE FORMS AND STRENGTHS ----------
30% Injectable Emulsion:
- 150 g/500 mL (0.3 g/mL) of lipid in Pharmacy Bulk Package (3)

----------CONTRAINDICATIONS----------
- Known hypersensitivity to egg, soybean, or peanut, or any of the active ingredients or excipients. (4, 5.3)
- Severe disorders of lipid metabolism characterized by hypertriglyceridemia (serum triglyceride > 1,000 mg/dL). (4, 5.7)

----------WARNINGS AND PRECAUTIONS----------
- Risk of Clinical Decompensation with Rapid Infusion of Intravenous Lipid Emulsion in Neonates and Infants: Acute respiratory distress, metabolic acidosis, and death after rapid infusion of intravenous lipid emulsions have been reported. When Intralipid 30% is diluted to 20%, strictly adhere to the recommended total daily dosage; the hourly infusion rate should not exceed 0.125 g/kg/hour for neonates and infants. (5.1, 8.4)
- Risk of Parenteral Nutrition-Associated Liver Disease (PNALD): Increased risk in patients who receive PN for extended periods of time, especially preterm neonates. Monitor liver function tests; if abnormalities occur consider discontinuation or dosage reduction. (5.2, 6.1, 8.4)
- Hypersensitivity Reactions: Monitor for signs or symptoms. Discontinue infusion if reactions occur. (5.3)
- Risk of Infections, Fat Overload Syndrome, Refeeding Syndrome, and Hypertriglyceridemia: Monitor for signs and symptoms; monitor laboratory parameters. (5.4, 5.5, 5.6, 5.7)
- Aluminum Toxicity: Increased risk in patients with renal impairment, including preterm neonates. (5.8, 8.4)

----------ADVERSE REACTIONS----------
Most common adverse drug reactions (≥5%) from clinical trials in adults were nausea, vomiting, and pyrexia. Most common adverse drug reactions (≥5%) from clinical trials in pediatric patients were anemia, vomiting, increased gamma-glutamyltransferase, and cholestasis. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Fresenius Kabi USA, LLC at 1-800-551-7176 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------
Vitamin K Antagonists (e.g., warfarin): Anticoagulant activity may be counteracted; increase monitoring of coagulation parameters. (7)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 7/2025

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Intralipid® is indicated as a source of calories and essential fatty acids for adult and pediatric patients requiring parenteral nutrition and as a source of essential fatty acids for prevention of essential fatty acid deficiency (EFAD).

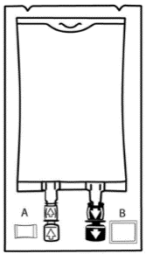
2 DOSAGE AND ADMINISTRATION

2.1 Important Preparation and Administration Instructions

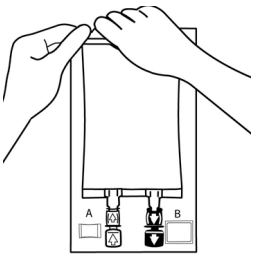
- Intralipid 30% Pharmacy Bulk Package is for admixing use only and is **not** intended for direct intravenous administration.
- Admixtures containing Intralipid 30% are prepared and administered by a healthcare provider in the inpatient setting *[see Dosage and Administration (2.2)].*
- Patients and caregivers may administer admixtures containing Intralipid for home use after appropriate training by a trained healthcare provider *[see Patient Counseling Information (17)].*
- Intralipid 30% must be combined with other PN fluids so that the resulting admixture has a final lipid concentration of no more than 20% (0.2 g lipid per mL of admixture). Refer to Admixture Preparation Instructions [*see Dosage and Administration (2.2)*].
- When Intralipid 30% is diluted to 20%, strictly adhere to the recommended total daily dosage; the hourly infusion rate should not exceed 0.125 g/kg/hour for neonates and infants *[see Warnings and Precautions (5.1)].*
- Intralipid admixtures with osmolarity
  - Greater than or equal to 900 mOsm/L must be infused through a central vein.
  - Less than 900 mOsm/L may be administered either through a central or peripheral vein.
- Use a 1.2 micron in-line filter during admixture administration.
- PN admixtures should use a dedicated infusion line without any connections. Do not connect multiple medications in series.
- To prevent air embolism, use a non-vented infusion set or close the vent on a vented set and fully evacuate residual gas in the bag prior to admixture administration.
- The flow rate of the admixture should be controlled with an infusion pump. Do not pressurize the flexible bag to increase flow rates, and if administration is controlled by a pumping device, turn off the pump before the bag runs dry.
- Do not use infusion sets and lines that contain di-2-ethylhexyl phthalate (DEHP), including infusion sets that contain polyvinyl chloride (PVC) components, because they contain DEHP as a plasticizer.
- After connecting the infusion set, start infusion of PN admixture with Intralipid immediately. Complete the infusion within 24 hours.

2.2 Admixture Preparation Instructions

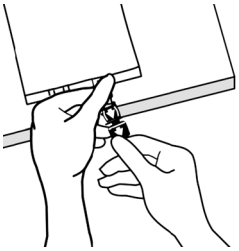
Use the following instructions to prepare the Intralipid 30% Pharmacy Bulk Package for transfer to a compounding bag:



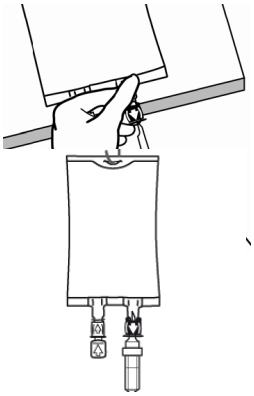
1. Inspect Bag
    - Inspect the integrity indicator (Oxalert®) (A) before removing the overpouch.
    - Discard the product if the indicator is black, overpouch is opened or damaged, emulsion color is not white, or seals of bag are broken.



2. Remove Overpouch
    - Place the bag on a clean, flat surface.
    - Tear the overpouch at notch and pull down.
    - Discard the Oxalert sachet (A) and the oxygen absorber (B).
    - Visually inspect the bag and contents for particulate matter and discoloration prior to administration. The lipid emulsion should be a homogenous liquid with a milky white appearance. If the mixture is not white or the emulsion has separated (noted by discoloration, phase separation, or oily droplets), or if particulates and/or leakage are observed, discard the bag.



3. Spike Bag
    - Identify the infusion port (**blue** cap with the arrow pointing away from the bag).
    - Immediately before inserting the compounding set, break off the **blue** infusion port cap.
    - Use a suitable sterile transfer device or dispensing set with an external spike diameter of 5.5 to 5.7 mm.
    - Hold the base of the infusion port.
    - Insert the spike through the infusion port by rotating your wrist slightly until the spike is inserted.
    - Do not pierce the infusion port more than once.



4. Transfer to the Compounding Bag
    - Hang the bag using the hanger cut and **start transfer to the compounding bag.**
    - Discard unused portion.

- Use the Intralipid 30% immediately for admixing after removal from the overpouch. If not used immediately, the product can be stored for no longer than 24 hours at 2°C to 8°C (36°F to 46°F). After removal from storage, and once the closure is penetrated, use Pharmacy Bulk Package contents within 4 hours.

- 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% intravenous lipid emulsions. Therefore, diluents other than dextrose and amino acids should not be used to prepare admixtures for direct intravenous administration.

Admixing Instructions

- Prepare the admixture in PN containers using strict aseptic techniques to avoid microbial contamination.
- Do not add Intralipid 30% Pharmacy Bulk Package to the PN container first; destabilization of the lipid may occur. The prime destabilizers of emulsions are excessive acidity (such as a pH <5) and inappropriate electrolyte content. Amino acid solutions exert buffering effects that protect the emulsion from destabilization. Give careful consideration to the addition of divalent cations (Ca++ and Mg++), which have been shown to cause emulsion instability.
- Do not inject additives directly into Intralipid.
- Intralipid 30% may be mixed with amino acid and dextrose injections to produce "all-in-one" PN admixtures. The mixing sequence below must be followed for manual compounding to minimize pH-related problems by ensuring that typically acidic dextrose injections are not mixed with lipid emulsions alone; shake bags gently after each addition.
    - Transfer dextrose injection to the PN container.
    - Transfer amino acid injection.
    - Transfer Intralipid 30%.
- Simultaneous transfer of amino acid injection, dextrose injection, and Intralipid to the PN container is also permitted; follow automated compounding device instructions as indicated. Use gentle agitation during admixing to minimize localized concentration effects.
- Additions to the PN admixtures should be evaluated by a pharmacist for compatibility. Questions about compatibility may be directed to Fresenius Kabi.
- Inspect the admixture to ensure that precipitates have not formed during preparation of the admixture and the emulsion has not separated. Discard the admixture if any of the above are observed.
- Infuse admixtures containing Intralipid immediately. If not used immediately, store admixtures under refrigeration at 2°C to 8°C (36°F to 46°F) for no longer than 24 hours. Infusion must be complete within 24 hours after removal from refrigeration. Discard any remaining admixture.
- Protect the admixed PN solution from light.

2.3 Recommended Dosage and Administration

- The recommended nutritional requirements of lipid and recommended dosages of Intralipid to be administered to meet those requirements for adults and pediatric patients are provided in Table 1.
- The dosing of Intralipid depends on the patient's individual energy requirements influenced by age, body weight, tolerance, clinical status, and the ability to metabolize and eliminate lipids.
- When determining dose, energy supplied by dextrose and amino acids from PN, as well as

energy from oral or enteral nutrition, has to be taken into account. Energy and lipid provided from lipid-based medications should also be taken into account (e.g., propofol).

- Prior to administration of admixtures with Intralipid, correct severe fluid and electrolyte disorders and measure serum triglyceride levels to establish a baseline value. In patients with elevated triglyceride levels, initiate Intralipid at a lower dosage and titrate in smaller increments, monitoring the triglyceride levels with each adjustment *[see Warnings and Precautions (5.7)]*.

Table 1: Recommended Pediatric and Adult Dosage for Intralipid concentrations of 20% or less in an admixture

Age	**Nutritional Requirements**
	Recommended Initial Dosage and Maximum Dosage
Birth to 2 years of age (including preterm and term neonates*) *[see Warnings and Precautions (5.1)]*	Initial 0.5 g/kg/day not to exceed 3 g/kg/day**
Pediatric patients 2 to <12 years of age	Initial 1 to 2 g/kg/day not to exceed 2.5 g/kg/day**
Pediatric patients 12 to 17 years of age	Initial 1 g/kg/day not to exceed 2 g/kg/day**
Adults	1 g/kg/day in stable patients ≤1 g/kg/day in critically ill patients not to exceed 2.5 g/kg/day**

* The neonatal period is defined as including term, post-term, and preterm neonates. The neonatal period for term and post-term neonates is the day of birth plus 27 days. For preterm neonates, the neonatal period is defined as the day of birth through the expected age of delivery plus 27 days (i.e., 44 weeks post-menstrual age).

** Daily dosage should also not exceed a maximum of 60% of total energy requirements *[see Overdosage (10)]*.

Dosage Modifications in Patients with Essential Fatty Acid Deficiency

When admixtures with Intralipid are administered to correct essential fatty acid deficiency (EFAD), supply 8% to 10% of caloric input from Intralipid in order to provide adequate amounts of linoleic and linolenic acids.

3 DOSAGE FORMS AND STRENGTHS

Intralipid 30% is a sterile, homogenous, milky, white lipid injectable emulsion in Flexible Containers supplied as:

- 150 g/500 mL (0.3 g/mL) of lipid in 500 mL Pharmacy Bulk Package

4 CONTRAINDICATIONS

- Known hypersensitivity to egg, soybean, peanut, or any of the active or inactive ingredients in Intralipid *[see Warnings and Precautions (5.3)]*
- Severe disorders of lipid metabolism characterized by hypertriglyceridemia (serum triglyceride >1,000 mg/dL) *[see Warnings and Precautions (5.7)]*

5 WARNINGS AND PRECAUTIONS

5.1 Clinical Decompensation with Rapid Infusion of Intravenous Lipid Emulsions in Neonates and Infants

In the postmarketing setting, serious adverse reactions including acute respiratory distress, metabolic acidosis, and death have been reported in neonates and infants after rapid infusion of intravenous lipid emulsions. Hypertriglyceridemia was commonly reported.

Intralipid 30% Pharmacy Bulk Package is not intended for direct infusion. When it is diluted to 20%, strictly adhere to the recommended total daily dosage; the hourly infusion rate should not exceed 0.125 g/kg/hour.

Preterm and small for gestational age infants have poor clearance of intravenous lipid emulsion and increased free fatty acid plasma levels following lipid emulsion infusion.

Carefully monitor the infant's ability to eliminate the infused lipids from the circulation (e.g., measure serum triglycerides and/or plasma free fatty acid levels). If signs or poor clearance of lipids from the circulation occur, stop the infusion and initiate a medical evaluation *[see Warnings and Precautions (5.5, 5.7) and Overdosage (10)]*.

5.2 Parenteral Nutrition-Associated Liver Disease and Other Hepatobiliary Disorders

Risk of Parenteral Nutrition-Associated Liver Disease

Parenteral nutrition-associated liver disease (PNALD), also referred to as intestinal failure-associated liver disease (IFALD), can present as cholestasis or hepatic steatosis, and may progress to steatohepatitis with fibrosis and cirrhosis (possibly leading to chronic hepatic failure). The etiology of PNALD is multifactorial; however, intravenously administered phytosterols (plant sterols) contained in plant-derived lipid emulsions, including Intralipid, have been associated with development of PNALD.

In a randomized study of neonates and infants expected to be treated with PN for at least 28 days, parenteral nutrition-associated cholestasis (PNAC), a precursor to PNALD, developed more frequently in Intralipid-treated patients than patients treated with a 4-oil mixed lipid emulsion. *[see Adverse Reactions (6.1), Use in Specific Populations (8.4)]*.

Monitor liver tests in patients treated with admixtures containing Intralipid and consider discontinuation or dosage reduction if abnormalities occur.

Other Hepatobiliary Disorders
Hepatobiliary disorders including cholecystitis and cholelithiasis have developed in some PN-treated patients without preexisting liver disease.

Monitor liver tests when administering admixtures containing Intralipid. Patients developing signs of hepatobiliary disorders should be assessed early to determine whether these conditions are related to Intralipid use.

5.3 Hypersensitivity Reactions

Intralipid contains soybean oil and egg phospholipids, which may cause hypersensitivity reactions. Cross reactions have been observed between soybean and peanut. In postmarketing experience, anaphylaxis has been reported following Intralipid administration *[see Adverse Reactions (6.2)]*.

Intralipid is contraindicated in patients with known hypersensitivity to egg, soybean, peanut or any of the active or inactive ingredients in Intralipid *[see Contraindications (4)]*. If a hypersensitivity reaction occurs, stop infusion of admixtures containing Intralipid immediately and initiate appropriate treatment and supportive measures.

5.4 Infections

Parenteral nutrition, such as Intralipid, can support microbial growth and is an independent risk factor for the development of catheter-related bloodstream infections. To decrease the risk of infectious complications, ensure aseptic techniques are used for catheter placement, catheter maintenance, and preparation and administration of admixtures containing Intralipid.

Monitor for signs and symptoms of infection including fever and chills, as well as laboratory test results that might indicate infection (including leukocytosis and hyperglycemia). Perform frequent checks of the intravenous catheter insertion site for edema, redness, and discharge.

5.5 Fat Overload Syndrome

Fat overload syndrome is a rare condition that has been reported with intravenous lipid injectable emulsions and is characterized by a sudden deterioration in the patient's condition (e.g., fever, anemia, leukopenia, thrombocytopenia, coagulation disorders, hyperlipidemia, hepatomegaly, deteriorating liver function, and central nervous system manifestations such as coma). A reduced or limited ability to metabolize lipids, accompanied by prolonged plasma clearance (resulting in higher lipid levels), may result in this syndrome. Although fat overload syndrome has been most frequently observed when the recommended lipid dose or infusion rate was exceeded, cases have also been described when the lipid formulation was administered according to instructions.

If signs or symptoms of fat overload syndrome occur, stop the infusion of admixtures containing Intralipid. The syndrome is usually reversible when the infusion of the lipid emulsion is stopped.

5.6 Refeeding Syndrome

Administering PN to severely malnourished patients may result in refeeding syndrome, which is characterized by the intracellular shift of potassium, phosphorus, and magnesium as patients become anabolic. Thiamine deficiency and fluid retention may also develop. To prevent these complications, closely monitor severely malnourished patients and slowly increase their nutrient intake.

5.7 Hypertriglyceridemia

The use of Intralipid is contraindicated in patients with hypertriglyceridemia with serum triglyceride concentrations >1,000 mg/dL.

Patients with conditions such as inherited lipid disorders, obesity, diabetes mellitus, or metabolic syndromes have a higher risk of developing hypertriglyceridemia with the use of Intralipid. In addition, patients with hypertriglyceridemia may have worsening of their hypertriglyceridemia with administration of Intralipid. Excessive dextrose administration may further increase such risk.

Evaluate patients' capacity to metabolize and eliminate the infused lipid emulsion by measuring serum triglycerides before the start of infusion (baseline value) and regularly throughout treatment. If triglyceride levels are above 400 mg/dL in adults, stop the Intralipid infusion and monitor serum triglyceride levels to avoid clinical consequences of hypertriglyceridemia such as pancreatitis. In pediatric patients with hypertriglyceridemia, lower triglyceride levels (i.e., below 400 mg/dL) may be associated with adverse reactions. Monitor serum triglyceride levels to avoid potential complications with hypertriglyceridemia such as pancreatitis, lipid pneumonitis, and neurologic changes, including kernicterus.

To minimize the risk of new or worsening of hypertriglyceridemia, assess high-risk patients for their overall energy intake including other sources of lipids and dextrose, as well as concomitant drugs that may affect lipid and dextrose metabolism.

5.8 Aluminum Toxicity

Intralipid contains no more than 25 mcg/L of aluminum. Prolonged PN administration in patients with renal impairment may result in aluminum reaching toxic levels. Preterm neonates are at greater risk because their kidneys are immature, and they require large amounts of calcium and phosphate solutions that contain aluminum.

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

5.9 Monitoring/Laboratory Tests

Monitor fluid status closely in patients with pulmonary edema or heart failure.

Throughout treatment, monitor serum triglycerides *[see Warnings and Precautions (5.7)],* essential fatty acids, fluid and electrolyte status, serum osmolarity, blood glucose, liver and kidney function, blood count (including platelets), and coagulation parameters.

The lipids contained in Intralipid may interfere with some laboratory tests (e.g., hemoglobin, lactate dehydrogenase, bilirubin, oxygen saturation) if blood is sampled before lipids have cleared from the bloodstream. Conduct these tests at least 6 hours after stopping the infusion.

Intralipid contains vitamin K that may counteract anticoagulant activity *[see Drug Interactions (7)]*.

6 ADVERSE REACTIONS

Adverse reactions described elsewhere in this Prescribing Information are:

- Clinical Decompensation with Rapid Infusion of Intravenous Lipid Emulsion in Neonates and Infants *[see Warnings and Precautions (5.1)]*
- Parenteral Nutrition-Associated Liver Disease and Other Hepatobiliary Disorders *[see Warnings and Precautions (5.2)]*
- Hypersensitivity Reactions *[see Warnings and Precautions (5.3)]*
- Infections *[see Warnings and Precautions (5.4)]*
- Fat Overload Syndrome *[see Warnings and Precautions (5.5)]*
- Refeeding Syndrome *[see Warnings and Precautions (5.6)]*
- Hypertriglyceridemia *[see Warnings and Precautions (5.7)]*
- Aluminum Toxicity *[see Warnings and Precautions (5.8)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

Intralipid 20% or equivalent soybean oil lipid emulsions functioned as the comparator in trials of the 4-oil mixed lipid emulsion *[see Clinical Studies (14)].* The adverse reactions from these studies are included to present the clinical experience with Intralipid because Intralipid 30% is to be diluted down to 20% or lower for PN admixture.

The safety database for Intralipid or equivalent soybean oil lipid emulsion exposure in these studies include 393 patients (230 adults; 163 pediatric) in 9 clinical trials. Adult patients were exposed for 5 days to 4 weeks in 5 clinical trials. Intralipid or equivalent soybean oil lipid emulsion was used as a component of PN which also included dextrose, amino acids, vitamins, and trace elements. Two of the 5 studies in adults were performed with Intralipid as a component of PN delivered in a 3-chamber bag.

Table 2: Adverse Reactions in >1% of Adult Patients Treated with Intralipid/Soybean Oil Emulsion

Adverse Reaction	Number of Patients in Soybean Oil Lipid Emulsion Group (N=230)	Number of Patients in 4-Oil Mixed Lipid Emulsion Comparator Group (N=229)
Nausea	26 (11%)	20 (9%)
Vomiting	12 (5%)	15 (7%)
Pyrexia	11 (5%)	9 (4%)
Hypertension	9 (4%)	6 (3%)
Headache	7 (3%)	3 (1%)
Hyperglycemia	5 (2%)	12 (5%)
Abdominal pain	5 (2%)	8 (4%)
Flatulence	4 (2%)	10 (4%)
Blood triglycerides increased	4 (2%)	6 (3%)
Sepsis	4 (2%)	5 (2%)
Diarrhea	4 (2%)	3 (1%)
Pneumonia	4 (2%)	3 (1%)
Pruritus	4 (2%)	3 (1%)
Gamma-glutamyltransferase increased	4 (2%)	2 (1%)

Less common adverse reactions occurring in ≤1% of adult patients who received Intralipid or equivalent soybean oil lipid emulsion were dyspepsia, urinary tract infection, anemia, infection, dyspnea, cholestasis, dysgeusia, increased blood alkaline phosphatase, tachycardia, liver function test abnormalities, dizziness, rash, and thrombophlebitis.

The 163 patients treated with Intralipid in four pediatric trials consisted of 147 patients <28 days of age, 9 patients 28 days to <2 years of age, and 7 patients 2 to 7 years of age; the duration of exposure was 7 to 84 days. Fifty-six percent of the pediatric patients were female, and 85% were Caucasian. Most pediatric patients were preterm neonates with feeding intolerance or other conditions requiring short-term (<29 days) PN.

Table 3: Adverse Reactions in >1% of Pediatric Patients Treated with Intralipid

Adverse Reaction	Number of Patients in Intralipid Group (N=163)	Number of Patients in 4-Oil Mixed Lipid Emulsion Comparator Group (N=170)
Anemia	33 (20%)	30 (18%)
Vomiting	16 (10%)	16 (9%)
Gamma-glutamyltransferase increased	12 (7%)	10 (6%)
Cholestasis	10 (6%)	7 (4%)
Pyrexia	7 (4%)	7 (4%)
C-reactive protein increased	7 (4%)	6 (4%)
Hyperbilirubinemia	7 (4%)	5 (3%)
Bilirubin conjugated increased	7 (4%)	3 (2%)
Nosocomial infection	6 (4%)	10 (6%)
Blood alkaline phosphatase increased	6 (4%)	1 (1%)
Abdominal pain	5 (3%)	4 (2%)
Hematocrit decreased	5 (3%)	2 (1%)
Metabolic acidosis	5 (3%)	2 (1%)
Diarrhea	4 (3%)	3 (2%)
Tachycardia	4 (3%)	3 (2%)
Thrombocytopenia	4 (3%)	3 (2%)
Alanine aminotransferase increased	3 (2%)	1 (1%)
Aspartate aminotransferase increased	3 (2%)	0 (0%)
Parenteral nutrition-associated liver disease	3 (2%)	0 (0%)

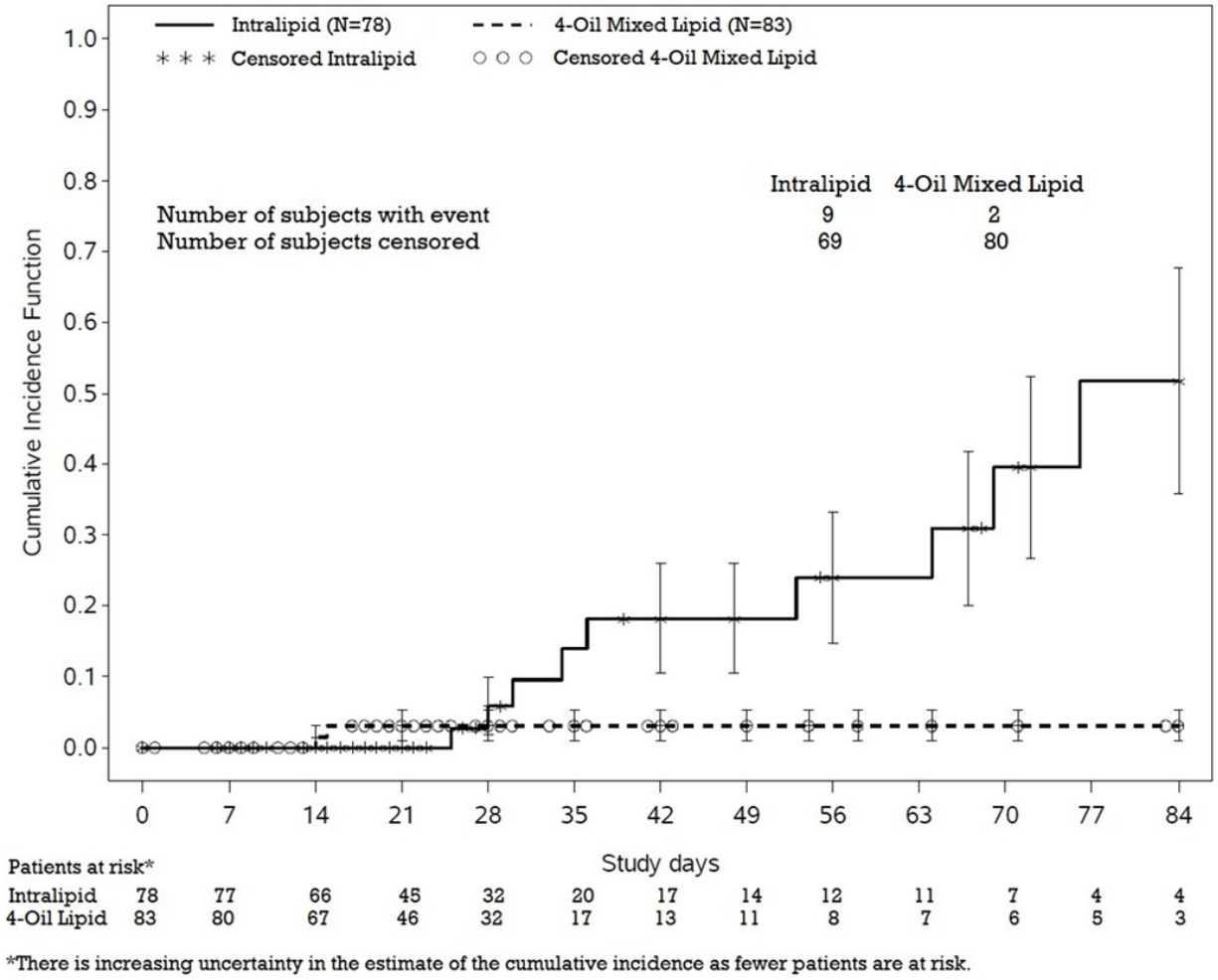
Less common adverse reactions occurring in ≤1% of pediatric patients who received Intralipid were hyperglycemia, sepsis, increased blood triglycerides, infection, fluid overload, hypertension, hypertriglyceridemia, rash, and hyperlipidemia.

In a randomized active-controlled, double-blind, parallel-group, multi-center study that included 152 neonates and 9 patients ranging in age from 29 to 153 days who were expected to require PN for at least 28 days, PNAC, a precursor to PNALD, developed more frequently in Intralipid-treated patients than in patients treated with a comparator 4-oil mixed lipid emulsion.

PNAC (defined as direct bilirubin >2 mg/dL with a second confirmed elevation >2 mg/dL at least 7 days later) occurred in 11.5% (9/78) in Intralipid-treated patients and 2.4% (2/83) of patients treated with a 4-oil mixed lipid emulsion. Most PNAC events occurred in patients who were treated for longer than 28 days.

The estimated cumulative incidence of PNAC is shown in the Kaplan-Meier cumulative incidence curve in Figure 1 *[see Pediatric Clinical Studies (14.2)]*.

Figure 1: Cumulative Incidence Curve of Time to Parenteral Nutrition-Associated Cholestasis (PNAC) with Standard Error Bars



*There is increasing uncertainty in the estimate of the cumulative incidence as fewer patients are at risk.

6.2 Postmarketing Experience

The following adverse reactions from voluntary reports have been reported with Intralipid. Because many of these reactions were reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Cardiac disorders: palpitations
Gastrointestinal disorders: vomiting, nausea
General disorders and administration site conditions: chills, chest discomfort, pyrexia
Nervous system disorders: dizziness
Respiratory, thoracic, and mediastinal disorders: dyspnea
Immune system disorders: hypersensitivity reactions, including anaphylaxis *[see Contraindications (4), Warnings and Precautions (5.3)]*.

Vascular disorders: phlebitis
Blood and lymphatic system disorders: hypercoagulability

7 DRUG INTERACTIONS

Soybean oil in Intralipid contains vitamin K_1 which may counteract the anticoagulant activity of vitamin K antagonists such as warfarin. In patients who receive concomitant Intralipid and warfarin, increase monitoring of laboratory parameters for anticoagulant activity.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary
Administration of the recommended dose of Intralipid is not expected to cause major birth defects, miscarriage, or other adverse maternal or fetal outcomes. No animal reproduction studies have been conducted with Intralipid. There are risks to the fetus associated with severe malnutrition during pregnancy *(see Clinical Considerations)*.

The background risk of major birth defects and miscarriage for the indicated population(s) is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Clinical Considerations
Disease-Associated Maternal and/or Embryo-Fetal Risk
Severe malnutrition in pregnant women is associated with preterm delivery, low birth weight, intrauterine growth restriction, congenital malformations, and perinatal mortality. Parenteral nutrition should be considered if the pregnant woman's nutritional requirements cannot be fulfilled by oral or enteral intake.

8.2 Lactation

Risk Summary
Administration of the recommended dose of Intralipid is not expected to cause harm to a breastfed infant. There are no data on the presence of Intralipid in human or animal milk or its effects on milk production. Available published literature includes fewer than five reported cases of breastfed infants exposed to various lipid emulsions via lactation, and these cases did not report adverse events. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Intralipid and any potential adverse effects of Intralipid on the breastfed infant, or from the underlying maternal condition.

8.4 Pediatric Use

Intralipid is contraindicated in pediatric patients with severe disorders of lipid metabolism [*(see Contraindications (4)]*.

The safety and effectiveness of Intralipid have been established as a source of calories and essential fatty acids for PN in pediatric patients, including term and preterm neonates. Use of Intralipid in neonates is supported by evidence from short-term (i.e., 1- to 4- week) studies, and one study following neonates beyond 4 weeks *[see Clinical Studies (14.2)]*. Use of Intralipid in older pediatric patients is supported by evidence from short-term (i.e., <28 days) studies in pediatric patients 28 days to 12 years of age and additional evidence from studies in adults *[see Clinical Studies (14)]*. The most common adverse reactions in Intralipid-treated pediatric patients were anemia, vomiting, gamma-glutamyltransferase increased, and cholestasis. PNAC, a precursor to PNALD, developed more frequently in Intralipid-treated patients than in patients treated with a comparator 4-oil mixed lipid emulsion *[see Warnings and Precautions (5.1) and Adverse Reactions (6.1)]*.

In the postmarketing setting, clinical decompensation with rapid infusion of intravenous lipid emulsion in neonates and infants, sometimes fatal, has been reported *[see Warnings and Precautions (5.1)]*. Because of immature renal function, preterm neonates receiving prolonged treatment with Intralipid may be at risk for aluminum toxicity *[see Warnings and Precautions (5.8)]*.

8.5 Geriatric Use

Reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or drug therapy.

10 OVERDOSAGE

In the event of an overdose, serious adverse reactions may result *[see Warnings and Precautions (5.1, 5.5)]*. Stop the infusion of admixtures containing Intralipid until triglyceride levels have normalized and symptoms have abated. The effects are usually reversible by stopping the lipid infusion. If medically appropriate, further intervention may be indicated. Lipids are not dialyzable from plasma.

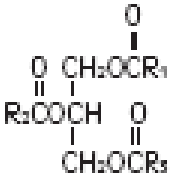
11 DESCRIPTION

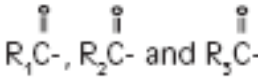
Intralipid is a sterile, non-pyrogenic, white, homogenous lipid emulsion for intravenous infusion as a source of calories and essential fatty acids for use in a pharmacy admixture program. The lipid content of Intralipid 30% Pharmacy Bulk Package is 0.3 g/mL and comprises soybean oil. The phosphate content is 15 mmol/L.

The total energy content, including fat, phospholipids, and glycerin is 3,000 kcal/L.

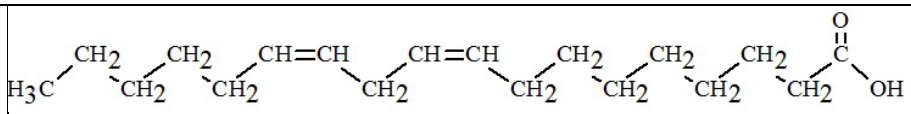
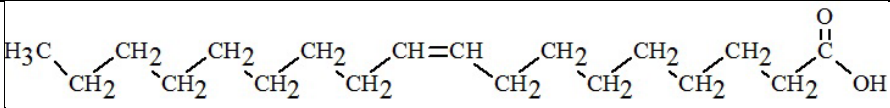
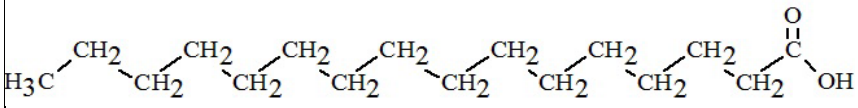
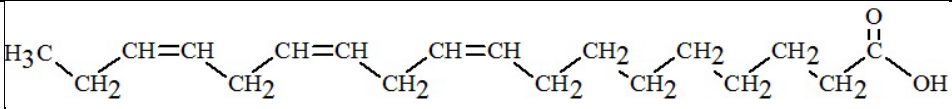
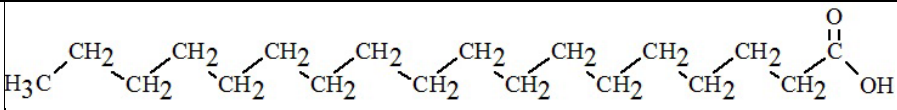
Each 100 mL of Intralipid contains approximately 30 g soybean oil, 1.2 g egg yolk phospholipids, 1.7 g glycerin, water for injection, and sodium hydroxide for pH adjustment (pH 6 to 8.9). Intralipid has an osmolality of approximately 310 mOsm/kg water (which represents an osmolarity of 200 mOsm/L).

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

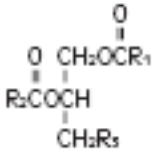


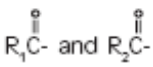
where  are saturated and unsaturated fatty acid residues.

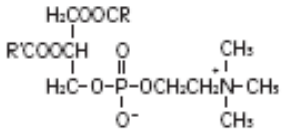
The major component fatty acids in Intralipid are linoleic acid (44% to 62%), oleic acid (19% to 30%), palmitic acid (7% to 14%), alpha-linolenic acid (4% to 11%), and stearic acid (1.4% to 5.5%). These fatty acids have the following chemical and structural formulas:

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 $C_{18}H_{36}O_2$	

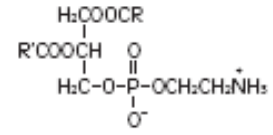
Purified egg phosphatides are a mixture of naturally occurring phospholipids which are isolated from the egg yolk. These phospholipids have the following general structure:



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

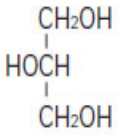


Phosphatidylcholine



Phosphatidylethanolamine

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



The container-solution 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 oxygen and moisture barrier when necessary.

Intralipid contains no more than 25 mcg/L of aluminum.

The container is not made with natural rubber latex, PVC, or DEHP.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Intralipid provides a biologically utilizable source of calories and essential fatty acids.

Fatty acids serve as an important substrate for energy production. The most common mechanism of action for energy production derived from fatty acid metabolism is beta oxidation. Fatty acids are also important for membrane structure and function, as precursors for bioactive molecules (such as prostaglandins), and as regulators of gene expression.

12.2 Pharmacodynamics

The pharmacodynamic effects of Intralipid have not been fully characterized.

12.3 Pharmacokinetics

Intralipid provides fatty acids in the form of triglycerides which are hydrolyzed by lipoprotein lipase to release free fatty acids. Linoleic acid and alpha-linolenic acid are metabolized within a common biochemical pathway through a series of desaturation and elongation steps.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity, genetic toxicology, and animal fertility studies have not been performed with Intralipid.

14 CLINICAL STUDIES

Intralipid 20% or equivalent soybean oil lipid emulsion functioned as the comparator for the 4-oil mixed lipid emulsion in the clinical studies described in sections 14.1 and 14.2. The trial results are included to present the clinical experience with Intralipid because Intralipid 30% is to be diluted downto 20% or lower for PN admixture.

14.1 Adult Clinical Studies

The efficacy of Intralipid or equivalent soybean oil lipid emulsion compared to a 4-oil mixed lipid emulsion was evaluated in 3 clinical studies in adult patients. Nutritional efficacy in adult studies was assessed by changes in anthropometric indices (body weight, height, and body mass index [BMI]), changes in lipid and protein metabolism (albumin), and fatty acid parameters. Of the 354 adult patients (178 Intralipid; 176 comparator), 62% were male, 99% were Caucasian, and ages ranged from 19 to 96 years. All patients received Intralipid/equivalent soybean oil lipid emulsion or the comparator as part of a PN regimen. Although Adult Study 1, Adult Study 2, and Adult Study 3 were not designed for formal statistical comparisons between Intralipid/equivalent soybean oil lipid emulsion and the comparator, they support Intralipid as a source of calories and essential fatty acids in adults. The lipid dosage was variable in these studies and adjusted to the patient's nutritional requirements.

Adult Study 1 was a double-blind, randomized, active-controlled, parallel-group, multicenter study in patients who required PN for at least 28 days. Seventy-five patients were enrolled, and 73 patients were treated with either Intralipid or the comparator. Changes in mean triglyceride levels from baseline values to Week 4 were similar in both the Intralipid and comparator groups. Mean albumin levels demonstrated a comparable decrease in both groups. Mean changes in body weight (kg) and BMI (kg/m2) were similar in both the Intralipid and the comparator groups.

Adult Study 2 was a phase 3, randomized, double-blind, active-controlled, multicenter study. A total of 249 postoperative adult patients were randomized to receive either an equivalent soybean oil lipid emulsion to Intralipid or the comparator for at least 5 days as part of their total parenteral nutrition (TPN) regimen. From baseline to Day 6, mean triglyceride levels increased similarly in both the soybean oil lipid emulsion and the comparator groups.

Adult Study 3 was a double-blind randomized, active-controlled, parallel-group, single-center study in 32 adult patients who required TPN for 10 to 14 days. Patients were treated with either an equivalent soybean oil lipid emulsion to Intralipid or the comparator. The increase in mean triglyceride levels from baseline to the final assessment was similar in both the soybean oil lipid emulsion and the comparator groups.

14.2 Pediatric Clinical Studies

The efficacy of Intralipid compared to a 4-oil mixed lipid emulsion in pediatric patients of all age groups, including term and preterm neonates, was evaluated in 333 patients in 4 randomized active-controlled, double-blind, parallel-group controlled clinical studies. Although Pediatric Studies 1, 2, 3, and 4 were not designed for formal statistical comparisons between Intralipid and the comparator, they support Intralipid as a source of calories and essential fatty acids in pediatric patients. The 333 pediatric patients (163 Intralipid; 170 comparator) consisted of 296 patients who were <28 days old, 22 patients 29 days to <2 years old, and 15 patients 2 to <12 years old. Fifty percent of the pediatric patients were male and 87% were Caucasian. All patients received Intralipid or the comparator as part of a PN regimen. Nutritional efficacy in neonates was assessed by changes in anthropometric indices (body weight, height, head circumference). Nutritional efficacy in pediatric patients, 28 days to 12 years of age, was assessed by changes in triglyceride concentrations and fatty acid parameters.

Pediatric Study 1 enrolled 152 preterm and term neonates (birth up to 28 days) and 9 patients ranging in age from 29 to 153 days. Patients were treated with either Intralipid (n=78) or the comparator (n=83). A total of 119 patients (58 Intralipid; 61 comparator) received study treatment for ≥14 days. A total of 27 patients received Intralipid for ≥29 days; 5 patients received Intralipid for the maximum study duration of 78-84 days.

Pediatric Studies 2 and 3 enrolled 60 and 84 preterm neonates, respectively, who were treated with either Intralipid or the comparator (72 neonates in each group). The median treatment duration for Intralipid group was 9 days in Pediatric Study 2 and 6 days in Pediatric Study 3.

Pediatric Study 4 enrolled 28 patients 5 months to <2 years of age and 15 patients 2 to 11.5 years of age. Patients were treated with either Intralipid (n=13) or the comparator (n=15) with a median treatment duration of 27 days.

In Pediatric Studies 1, 2 and 3, which enrolled neonates, Intralipid-treated patients showed increases in the median body weight, height/length, and head circumference (which was measured in Studies 1 and 3) comparable to the comparator-treated patients. Mean triglyceride levels from baseline to the final assessment in Pediatric Studies 1, 2, and 3 were variable in these neonates, but overall differences between groups were not considered clinically relevant. Mean triglyceride levels in Pediatric Study 4 were variable but remained within the normal range.

16 HOW SUPPLIED/STORAGE AND HANDLING

Intralipid 30% (lipid injectable emulsion, USP) is a sterile, homogeneous, milky, white lipid emulsion, supplied as Pharmacy Bulk Package in Flexible Containers.

Product Code	Each	Unit of Sale
831834311	NDC 65219-537-01 500 mL Pharmacy Bulk Package Bag	NDC 65219-537-50 Package of 12

Store below 25°C (77°F). Avoid excessive heat. Do not freeze. If accidentally frozen, discard container. Store in the overpouch until ready for use.

Use the Pharmacy Bulk Package immediately for admixing after removal from the overpouch. If not used immediately for admixing, the product should be stored for no longer than 24 hours at 2°C to 8°C (36°F to 46°F). After removal from storage, and once the closure is penetrated, use Pharmacy Bulk Package contents within 4 hours *[see Dosage and Administration (2.2)]*.

Admixtures

Infuse admixtures containing Intralipid immediately. If admixtures are not used immediately, admixtures should be stored at 2°C to 8°C (36°F to 46°F) for no longer than 24 hours. After removal from storage, infuse within 24 hours *[see Dosage and Administration (2.2)]*.

Protect the admixed PN solution from light *[see Dosage and Administration (2.2)]*.

17 PATIENT COUNSELING INFORMATION

When initiating administration of admixtures with Intralipid, discuss the following information with the patient or caregiver:

Clinical Decompensation with Rapid Infusion of Intravenous Lipid Emulsion in Neonates and Infants

Inform caregivers that acute respiratory distress and death may occur in neonates and infants after rapid infusion of intravenous lipid emulsions. If Intralipid is infused at home, instruct caregivers not to exceed the maximum infusion rate *[see Warnings and Precautions (5.1)]*.

Parenteral Nutrition-Associated Liver Disease and Other Hepatobiliary Disorders

Inform patients and caregivers that use of parenteral nutrition may result in parenteral nutrition-associated liver disease and/or other hepatobiliary disorders *[see Warnings and Precautions (5.2)]*.

Hypersensitivity Reactions

Inform patients and caregivers that Intralipid may cause hypersensitivity reactions, including anaphylaxis. If admixtures containing Intralipid are infused at home, instruct patients or caregivers to stop the infusion of admixtures containing Intralipid immediately and seek medical attention if they experience signs or symptoms of a hypersensitivity reaction, such as rapid or weak heartbeat, feeling faint, difficulty in breathing or swallowing, vomiting, nausea, headache, sweating, dizziness, hives, rash, itching, flushing, dizziness, fever, or chills *[see Warnings and Precautions (5.3)]*.

Infections

Inform patients and caregivers that patients who receive admixtures containing Intralipid are at risk of infection. If admixtures containing Intralipid are infused at home, instruct patients or caregivers to ensure aseptic techniques are used for the preparation and administration of

admixtures containing Intralipid and to monitor for signs and symptoms of infection *[see Warnings and Precautions (5.4)]*.

Fat Overload Syndrome

Inform patients and caregivers that fat overload syndrome has been reported with the use of intravenous lipid emulsions. If admixtures containing Intralipid are infused at home, instruct patients or caregivers to stop the infusion of admixtures containing Intralipid if signs or symptoms of fat overload syndrome occur *[see Warnings and Precautions (5.5)]*.

Refeeding Syndrome

If the patient is severely malnourished, inform patients and caregivers that administering parenteral nutrition including Intralipid may result in refeeding syndrome *[see Warnings and Precautions (5.6)]*.

Hypertriglyceridemia

Inform patients and their caregivers about the risks of hypertriglyceridemia with Intralipid use *[see Warnings and Precautions (5.7)]*.

Aluminum Toxicity

Inform patients and their caregivers that prolonged PN administration in patients with renal impairment, including preterm neonates, may result in aluminum reaching toxic levels associated with central nervous system and bone toxicity *[see Warnings and Precautions (5.8)]*.

Preparation and Administration Instructions

If it is acceptable for a patient or caregiver to administer admixtures containing Intralipid at home, then provide recommendations on how to inspect and prepare, add compatible additives (when appropriate), administer, and store admixtures containing Intralipid *[see Dosage and Administration (2.1, 2.2)]*. Inform patients or caregivers not to deviate from the administration instructions given by the healthcare provider.

Manufactured by:

Uppsala, Sweden

Intralipid® is a registered trademark of Fresenius Kabi AB.

www.fresenius-kabi.com/us

Package Insert Part Number Pending

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use KABIVEN safely and effectively. See full prescribing information for KABIVEN.

KABIVEN® (amino acids, electrolytes, dextrose and lipid injectable emulsion), for intravenous use
Initial U.S. Approval: 2014

----------RECENT MAJOR CHANGES----------
Warnings and Precautions (5.4) 7/2025

----------INDICATIONS AND USAGE----------
KABIVEN is indicated as a source of calories, protein, electrolytes and essential fatty acids for adult patients requiring parenteral nutrition when oral or enteral nutrition is not possible, insufficient, or contraindicated. KABIVEN may be used to prevent essential fatty acid deficiency or treat negative nitrogen balance in adult patients. (1)

Limitations of Use:
Not recommended for use in pediatric patients < 2 years including preterm infants because the fixed content of the formulation does not meet nutritional requirements in this age group. (1, 5.1, 8.4)

----------DOSAGE AND ADMINISTRATION----------
- For intravenous infusion only into a central vein. (2.1, 5.10)
- See full prescribing information regarding preparation, administration, instructions for use, the recommended dosage in adults, and dosage modifications for patients with renal impairment. (2.1, 2.2, 2.3, 2.4)

----------DOSAGE FORMS AND STRENGTHS----------
- KABIVEN is a sterile, hypertonic emulsion in a three-chamber container. The individual chambers contain one of the following: amino acids and electrolytes, dextrose, or lipid injectable emulsion. (3)
- KABIVEN is available in four sizes 2,566 mL, 2,053 mL, 1,540 mL and 1,026 mL. (3)

----------CONTRAINDICATIONS----------
- Concomitant treatment with ceftriaxone in neonates (28 days of age or younger). (4)
- Known hypersensitivity to egg, soybean, peanut or any of the active or inactive ingredients. (4)
- Severe disorders of lipid metabolism characterized by hypertriglyceridemia (with serum triglycerides >1,000 mg/dL. (4, 5.10)
- Inborn errors of amino acid metabolism. (4)
- Cardiopulmonary instability. (4)
- Hemophagocytic syndrome. (4)

----------WARNINGS AND PRECAUTIONS----------
- Clinical Decompensation with Rapid Infusion of Intravenous Lipid Emulsion in Neonates and Infants: Acute respiratory distress, metabolic acidosis, and death after rapid infusion of intravenous lipid emulsions have been reported. (5.1)
- Parenteral Nutrition-Associated Liver Disease: Increased risk in patients who receive parenteral nutrition for greater than 2 weeks. Monitor liver tests; if abnormalities occur, consider discontinuation or dosage reduction. (5.2)
- Pulmonary Embolism and Respiratory Distress due to Pulmonary Vascular Precipitates: If signs of pulmonary distress occur, stop the infusion and initiate a medical evaluation. (5.3)
- Hypersensitivity Reactions: Monitor for signs or symptoms and discontinue infusion if reactions occur. (5.4)
- Precipitation with Ceftriaxone: Do not administer ceftriaxone simultaneously with KABIVEN via a Y-site. (4, 5.5, 8.4)
- Infection, fat overload, hyperglycemia and refeeding complications: Monitor for signs and symptoms; monitor laboratory parameters. (5.6, 5.7, 5.8, 5.9, 5.14)

----------ADVERSE REACTIONS----------
The most common adverse reactions (≥3%) are nausea, pyrexia, hypertension, vomiting, decreased hemoglobin, decreased total protein, hypokalemia, decreased potassium, and increased gamma glutamyltransferase. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Fresenius Kabi USA, LLC at 1-800-551-7176 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------
Coumarin and coumarin derivatives, including warfarin: Anticoagulant activity may be counteracted; monitor laboratory parameters. (7.1)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 7/2025

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

KABIVEN is indicated as a source of calories, protein, electrolytes and essential fatty acids for adult patients requiring parenteral nutrition when oral or enteral nutrition is not possible, insufficient, or contraindicated. KABIVEN may be used to prevent essential fatty acid deficiency or treat negative nitrogen balance in adult patients.

Limitations of Use:

KABIVEN is not recommended for use in pediatric patients under the age of 2 years, including preterm infants because the fixed content of the formulation does not meet the nutritional requirements of this age group *[see Warnings and Precautions (5.1) and Use in Specific Populations (8.4)]*.

2 DOSAGE AND ADMINISTRATION

2.1 Administration

- KABIVEN is for intravenous infusion only into a central vein *[see Warnings and Precautions (5.11)]*.
- Use a 1.2 micron in-line filter.
- Use of a vented intravenous administration set with the vent in the open position could result in air embolism.
- Use a dedicated line without any connections. Multiple connections could result in air embolism due to residual air being drawn from the primary container before administration of the fluid from the secondary container is completed.
- Do not exceed the recommended maximum infusion rate of 2.6 mL/kg/hour *[see Dosage and Administration (2.4) and Warnings and Precautions (5.1)]*.
- Ceftriaxone must not be administered simultaneously with calcium-containing intravenous solutions such as KABIVEN via a Y-site due to precipitation. However, in patients other than neonates, ceftriaxone and KABIVEN may be administered sequentially if the infusion lines are thoroughly flushed between infusions with a compatible fluid *[see Contraindications (4), Warnings and Precautions (5.5)]*.
- Do not use administration sets and lines that contain di-2-ethylhexyl phthalate (DEHP). Administration sets that contain polyvinyl chloride (PVC) components have DEHP as a plasticizer.

2.2 Important Preparation Instructions

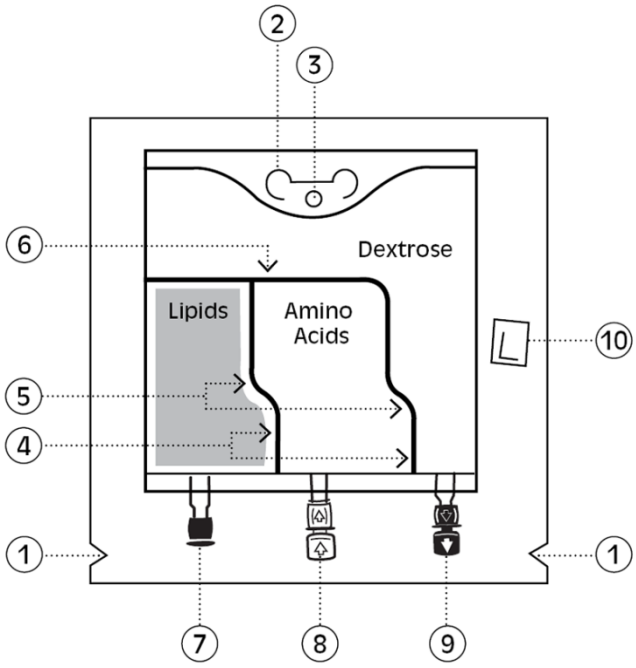
- Inspect the bag prior to activation. Discard the bag in the following situations:

- Evidence of damage to the bag
- More than one chamber is white
- Solution is yellow
- Any seal is already broken

- Activate the bag *[see Dosage and Administration (2.3)]*.
- Once the bag is activated, ensure the vertical seals between chambers are broken at least from the bend in the seals and down to the ports. The upper sections of the vertical seals above the bend and the horizontal seal may remain closed.
- It is recommended to mix the contents thoroughly by inverting the bag upside down to ensure a homogenous admixture.
- Ensure the vertical seals between chambers are broken and the contents of all three chambers are mixed together prior to infusion *[see Dosage and Administration (2.3)]*.
- Use KABIVEN immediately after the introduction of additives. If not used immediately, the storage time and conditions prior to use should not be longer than 24 hours at 2° to 8°C (36° to 46°F). After removal from storage at 2° to 8°C (36° to 46°F), the admixture should be infused within 24 hours. Any mixture remaining must be discarded.
- In the absence of additives, once activated, KABIVEN remains stable for 48 hours at 25°C (77°F). If not used immediately, the activated bag can be stored for up to 7 days under refrigeration [2° to 8°C (36º to 46°F)]. After removal from refrigeration, the activated bag should be used within 48 hours.
- For total parenteral nutrition add multivitamins and trace elements via the additive port. Any other additions to the bag should be evaluated by a pharmacist for compatibility. Questions about compatibility may be directed to Fresenius Kabi USA, LLC.
- When introducing additives, it is recommended to use 18 to 23 gauge needles with a maximum length of 1.5 inches (40 mm) and to mix thoroughly after each addition, use aseptic technique and add after the vertical seals have been broken (i.e. bag has been activated) and the three components are mixed *[see Dosage and Administration (2.3)]*.
- Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Inspect KABIVEN to ensure:
  - Precipitates have not formed during the mixing or addition of additives.
  - The emulsion has not separated. Separation of the emulsion can be visibly identified by a yellowish streaking or the accumulation of yellowish droplets in the mixed emulsion.

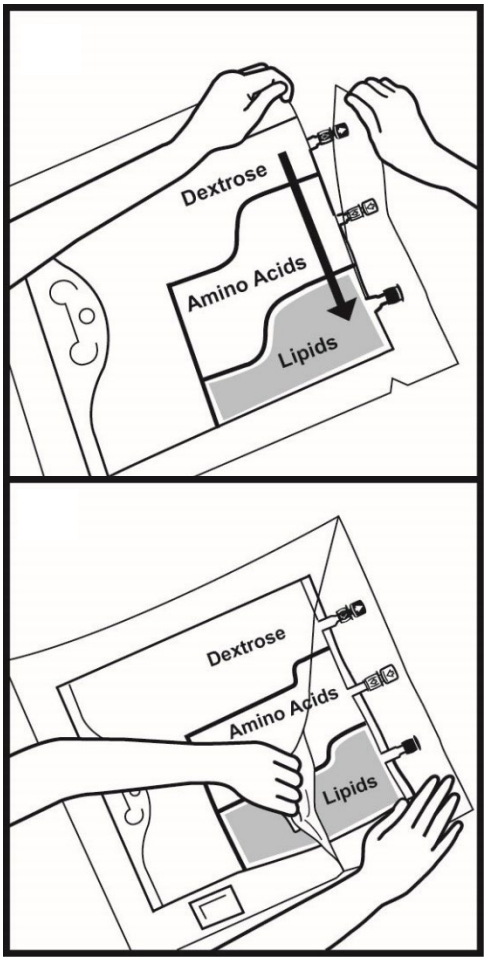
  Discard the admixture if any of the above are observed.

2.3 Instructions for Use



1. **Overpouch Notch**
2. **Handle**
3. **Hole** (For hanging the bag)
4. **Vertical Seals** (Must break to activate)
5. **Bends in Vertical Seals**
6. **Horizontal Seal** (May remain unopened)
7. **Blind Port** (NEVER use this port)
8. **WHITE Additive Port**
9. **BLUE Infusion Port**
10. **Oxygen Absorber** (Present between bag and inside overpouch-position may vary)

An instructional video is available at www.freseniuskabinutrition.com/products/kabiven-perikabiven/.



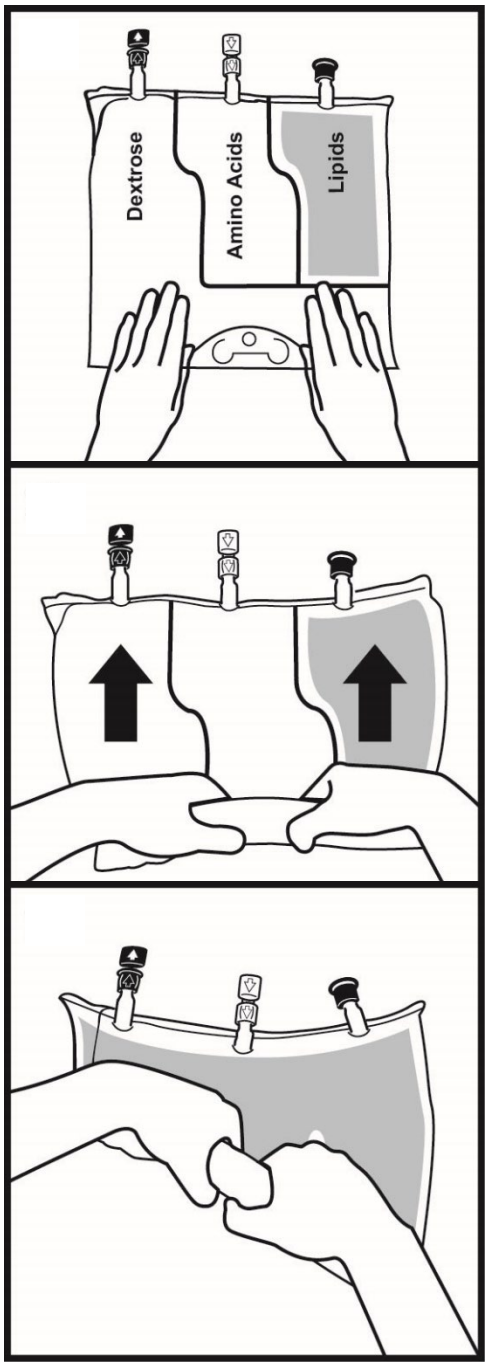
1. INSPECT BAG PRIOR TO ACTIVATION.

- KABIVEN is a 3 chambered bag:
  - One chamber is **WHITE**.
  - Two chambers are **CLEAR**.

a) Discard bag if:
- Overpouch is **OPENED OR DAMAGED.**
- More than one chamber is **WHITE**.
- Solution is **YELLOW**.
- Seals are already **BROKEN**.

2. REMOVE OVERPOUCH.

a) Place bag on a clean, flat surface.
b) Tear from Overpouch Notch, located close to the ports.
c) Tear long sides open to access the inner bag.
d) Discard Overpouch and Oxygen Absorber.



3. ACTIVATE BAG.

a) Place bag on a clean, flat surface with text side up and ports pointing away from you.

b) Roll ***tightly*** from top of bag down toward ports.

c) ***Apply pressure*** until both Vertical Seals break and entire contents are white. It may take up to 5 seconds of continued pressure to break Vertical Seals.

NOTE: Both Vertical Seals must be broken from bends to ports. Upper section of Vertical Seals and Horizontal Seal may remain unbroken.

d) After both Vertical Seals are broken, mix contents thoroughly by inverting the bag at least three times to ensure a homogenous mixture.

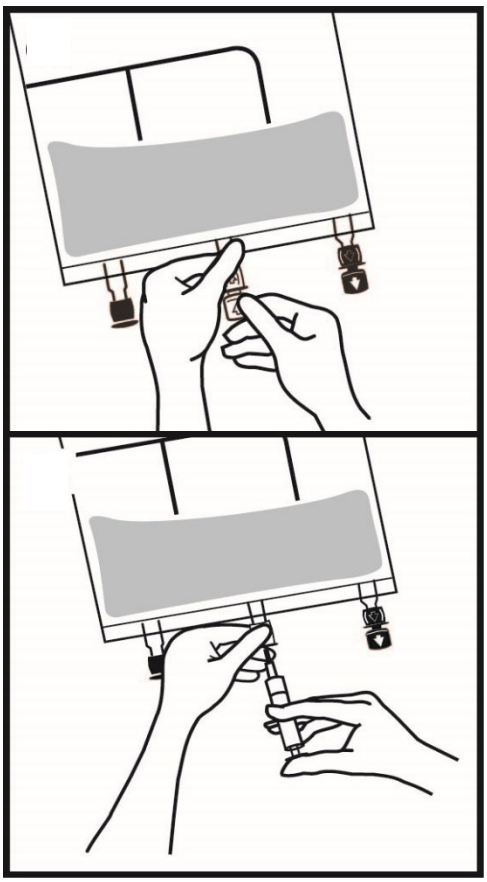
4. INSPECT BAG TO CONFIRM ACTIVATION.

- An activated bag has both Vertical Seals broken from bends to ports and entire contents are white.

5. IDENTIFY CORRECT PORT.

- Additive port is **WHITE** with arrow pointing toward bag.
- Infusion port is **BLUE** with arrow pointing away from bag.

Reference ID: 5630382

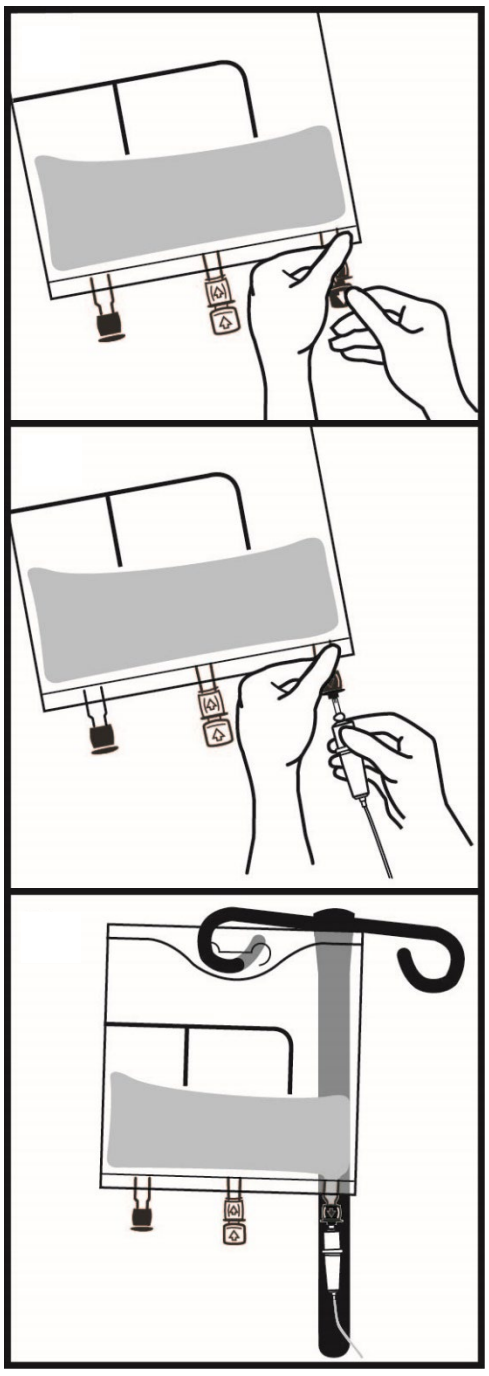


6. MAKE ADDITIONS (if prescribed).

WARNING: Ensure additives are compatible.

a) Immediately before injecting additives, break off **WHITE** Additive Port cap with the arrow pointing toward the bag.
b) Hold base of Additive Port horizontally.
c) Insert needle horizontally through the center of Additive Port's septum and inject additives.
d) Repeat as necessary using aseptic technique.
e) Mix thoroughly after each addition.

NOTE: The membrane of Additive Port is sterile at first use. Use aseptic technique for subsequent additions. The septum can be pierced up to 10 times with the recommended needle size 18 to 23 G 1½ inches (40mm).



7. SPIKE AND HANG BAG.

a) Immediately before inserting the infusion set, break off **BLUE** Infusion Port cap with the arrow pointing away from the bag.
b) Use a non-vented infusion set or close the air-inlet on a vented set. It is recommended to use 1.2 µm in-line filter.
c) Close the roller clamp of the infusion set.
d) Hold the base of Infusion Port.
e) Insert spike through Infusion Port by rotating your wrist slightly until the spike is inserted.
f) Lift and hold the bag with both hands.
g) Hang the bag by Hole below Handle.

NOTE: The membrane of Infusion Port is sterile at first use. Use infusion sets (according to ISO Number 8536-4) with an external spike diameter of 5.5 to 5.7 mm.

8. FOR SINGLE USE ONLY.

- Discard unused portion.

2.4 Dosing Considerations

The dosage of KABIVEN should be individualized based on the patient's clinical condition (ability to adequately metabolize amino acids, dextrose and lipids), body weight and nutritional/fluid requirements, as well as additional energy given orally/enterally to the patient.

KABIVEN is a combination of amino acids, electrolytes, dextrose, and lipids in a fixed volume and concentration. The dosage selection is based upon fluid requirements which can be used in conjunction with the nutritional requirements to determine final dosage [see Table 1]. KABIVEN meets the total nutritional requirements for protein, dextrose and lipids in stable patients, and can be individualized to meet specific needs with the addition of nutrients. The maximum infusion rate is based upon the dextrose component.

Prior to administration of KABIVEN, correct severe fluid, electrolyte and acid-base disorders. Before starting the infusion, obtain serum triglyceride levels to establish the baseline value.

Recommended Adult Dosage

The recommended dosage of KABIVEN in adults is 19 to 38 mL/kg/day. The amount of macronutrients provided by KABIVEN are shown in Table 1.

The maximum daily dosage of KABIVEN in adults should not exceed 40 mL/kg/day.
In patients with serum triglyceride concentrations above 400 mg/dL, stop the KABIVEN infusion and monitor serum triglyceride levels. Once the triglycerides are <400 mg/dL, restart KABIVEN at a lower infusion rate and advance rate in smaller increments towards target dosage, checking the triglyceride levels prior to each adjustment *[see Contraindications (4) and Warnings and Precautions (5.13)]*.

Table 1: Macronutrient Content of KABIVEN Based on Recommended Dosage

	Nutrition Provided by KABIVEN recommended dosage
Fluid mL/kg/day	19 to 38
Protein* g/kg/day Nitrogen g/kg/day	0.6 to 1.3 0.1 to 0.2
Dextrose** g/kg/day	2.1 to 4.1
Lipids g/kg/day	0.7 to 1.5
Total Energy Requirement kcal/kg/day	16 to 32

* Protein is provided as amino acids. When infused intravenously amino acids are metabolized and utilized as the building blocks of protein.

** As Dextrose monohydrate

Treatment with KABIVEN may be continued for as long as is required by the patient's condition.

Dosing in Renal Impairment

In patients with renal impairment, the dosage of KABIVEN should be the recommended adult dosage (see above). Prior to administration, correct severe fluid or electrolyte imbalances. Closely monitor serum electrolyte levels and adjust the volume of KABIVEN administered as required *[see Warnings and Precautions (5.12)]*.

Renal patients not needing dialysis require 0.6 to 0.8 g of protein/kg/day. Patients on dialysis or continuous renal replacement therapy should receive 1.2 to 1.8 g of protein/kg/day up to a maximum of 2.5 g of protein/kg/day based on nutritional status and estimated protein losses. The KABIVEN dosage can be adjusted based on the treatment for the renal impairment, supplementing protein as indicated. If required, additional amino acids may be added to the KABIVEN bag or infused separately.

Infusion Duration and Rate

The recommended duration of infusion for KABIVEN is between 12 and 24 hours, depending on the clinical situation.

The maximum infusion rate of KABIVEN is 2.6 mL/kg/hour. This corresponds to 0.09 g/kg/hour of amino acids, 0.28 g/kg/hour of dextrose (the rate limiting factor) and 0.1 g/kg/hour of lipids.

Dosing Instructions

1. Determine the fluid requirements (19 to 38 mL/kg/day) and the patient's nutritional requirements to be delivered, and then select the corresponding KABIVEN bag.
2. Determine the preferred duration of infusion (12 to 24 hours).
3. Ensure that the rate of infusion (KABIVEN dosage in mL/kg/day divided by the preferred duration of infusion (hours)) does not exceed the maximum infusion rate for the patient (i.e., 2.6 mL/kg/hour). The infusion rate may need to be reduced and duration of infusion increased in order not to exceed the maximum infusion rate.
4. Once the infusion rate in mL/kg/hour has been selected, calculate the infusion rate (mL/hour) using the patient's weight.
5. Compare the patient's nutrient requirements with the amount supplied by KABIVEN. Discuss with a pharmacist any additions that may be required.

3 DOSAGE FORMS AND STRENGTHS

KABIVEN is a sterile, hypertonic emulsion in a three-chamber container. The individual chambers contain one of the following respectively: amino acids and electrolytes, dextrose, or lipid injectable emulsion. Table 2 describes the individual components of KABIVEN.

Table 2: Contents of KABIVEN when mixed

How Supplied	2,566 mL	2,053 mL	1,540 mL	1,026 mL
Composition of KABIVEN				
Soybean Oil, USP (g/100 mL)			3.9	
Dextrose Monohydrate, USP (g/100 mL)			10.8	
Amino Acids, USP (g/100 mL)			3.31	
Total Nitrogen (mg/100 mL)			526	
Essential amino acids (mg/100 mL)	Lysine, USP (added as the hydrochloride salt)		263	
	Phenylalanine, USP		231	
	Leucine, USP		231	
	Valine, USP		213	
	Histidine, USP		199	
	Threonine, USP		164	
	Methionine, USP		164	
	Isoleucine, USP		164	
	Tryptophan, USP		55	
Nonessential amino acids (mg/100 mL)	Alanine, USP		467	
	Arginine, USP		330	
	Glycine, USP		231	
	Proline, USP		199	
	Glutamic Acid		164	
	Serine, USP		131	
	Aspartic Acid, USP		99	
	Tyrosine, USP		6.7	
Electrolytes (mg/100 mL)	Sodium Acetate Trihydrate, USP		239	
	Potassium Chloride, USP		174	
	Sodium Glycerophosphate Anhydrous		147	
	Magnesium Sulfate Heptahydrate, USP		96	
	Calcium Chloride Dihydrate, USP		29	
Electrolyte Profile[1] (mEq/L)	Sodium[2]		31 (31 mmol/L)	
	Potassium		23 (23 mmol/L)	
	Magnesium		7.8 (3.9 mmol/L)	
	Calcium		3.8 (1.9 mmol/L)	
	Phosphorous[3]		N.A. (9.7 mmol/L)	
	Acetate[4]		38 (38 mmol/L)	
	Chloride[5]		45 (45 mmol/L)	
	Sulfate[6]		7.8 (3.9 mmol/L)	
Calorie Content (kcal/L)	From Dextrose[9]		367	
	From Lipid		390[7]	
	From Amino Acids		132	
	Total		889	
pH[8]			5.6	
Osmolarity (mOsm/L)			1060	

1. Balanced by ions from amino acids
2. Contributed by sodium glycerophosphate and sodium acetate
3. Contributed by sodium glycerophosphate and phospholipids

4. Derived from sodium acetate and glacial acetic acid (for pH adjustment)
5. Contributed by calcium chloride, lysine hydrochloride, and potassium chloride
6. Derived from magnesium sulfate
7. Total caloric value including lipid, phospholipid and glycerin
8. pH of amino acid with electrolyte solution was adjusted with glacial acetic acid, USP and pH of lipid emulsion was adjusted with sodium hydroxide, USP
9. Calculated on the basis of 3.4 kcal/g of dextrose, monohydrate

4 CONTRAINDICATIONS

The use of KABIVEN is contraindicated in:

- Neonates (28 days of age or younger) receiving concomitant treatment with ceftriaxone, even if separate infusion lines are used, due to the risk of fatal ceftriaxone calcium salt precipitation in the neonate's bloodstream *[see Limitations of Use (1), Warnings and Precautions (5.5), Use in Specific Populations (8.4)]*.
- Patients with known hypersensitivity to egg, soybean, peanut or any of the active or inactive ingredients in KABIVEN *[see Warnings and Precautions (5.4)]*.
- Patients with severe disorders of lipid metabolism characterized by hypertriglyceridemia (serum triglyceride concentration >1,000 mg/dL) *[see Warnings and Precautions (5.10)]*.
- Patients with inborn errors of amino acid metabolism
- Patients with cardiopulmonary instability (including pulmonary edema, cardiac insufficiency, myocardial infarction, acidosis and hemodynamic instability requiring significant vasopressor support)
- Patients with hemophagocytic syndrome

5 WARNINGS AND PRECAUTIONS

5.1 Clinical Decompensation with Rapid Infusion of Intravenous Lipid Emulsion in Neonates and Infants

In the postmarketing setting, serious adverse reactions including acute respiratory distress, metabolic acidosis, and death have been reported in neonates and infants after rapid infusion of intravenous lipid emulsions. Hypertriglyceridemia was commonly reported.

Preterm and small for gestational age infants have poor clearance of intravenous lipid emulsion and increased free fatty acid plasma levels following lipid emulsion infusion.

5.2 Parenteral Nutrition-Associated Liver Disease and Other Hepatobiliary Disorders

Risk of Parenteral Nutrition-Associated Liver Disease

Parenteral nutrition-associated liver disease (PNALD), also referred to as intestinal failure-associated liver disease (IFALD), can present as cholestasis or hepatic steatosis, and may progress to steatohepatitis with fibrosis and cirrhosis (possibly leading to chronic hepatic failure). The etiology of PNALD is multifactorial; however, intravenously administered phytosterols (plant sterols) contained in plant-derived lipid emulsions, such as Intralipid (included in KABIVEN), have been associated with development of PNALD.

In a randomized study of neonates and infants expected to be treated with PN for at least 28 days, parenteral nutrition-associated cholestasis (PNAC), a precursor to PNALD, developed more frequently in Intralipid-treated patients than in patients treated with a 4-oil mixed lipid emulsion *[see Adverse Reactions (6.1), Use in Specific Populations (8.4)]*.

Monitor liver tests in patients treated with KABIVEN and consider discontinuation or dosage reduction if abnormalities occur.

Other Hepatobiliary Disorders

Hepatobiliary disorders including cholecystitis and cholelithiasis have developed in some PN-treated patients without preexisting liver disease.

Monitor liver tests when administering KABIVEN. Patients developing signs of hepatobiliary disorders should be assessed early to determine whether these conditions are related to KABIVEN use.

5.3 Pulmonary Embolism and Respiratory Distress due to Pulmonary Vascular Precipitates

Pulmonary vascular precipitates causing pulmonary emboli (including some fatalities) and respiratory distress have been reported in patients receiving parenteral nutrition.

Excessive addition of calcium and phosphate increases the risk of the formation of calcium phosphate precipitates; however, precipitates have been reported even in the absence of phosphate salt in the solution. Precipitation following passage through an in-line filter and suspected in vivo precipitate formation has also been reported.

Visually inspect the prepared solution, the infusion set, and catheter for precipitates, prior to administration as well as periodically during the administration. If signs of respiratory distress or pulmonary embolism occur, stop the KABIVEN infusion and initiate a medical evaluation.

5.4 Hypersensitivity Reactions

KABIVEN contains soybean oil, which may cause hypersensitivity reactions. Cross reactions have been observed between soybean and peanut. In postmarketing experience, anaphylaxis has been reported following KABIVEN administration *[see Adverse Reactions (6.2)]*.

KABIVEN is contraindicated in patients with known hypersensitivity to egg, soybean, peanut or any of the active or inactive ingredients in KABIVEN *[see Contraindications (4)]*. If a hypersensitivity reaction occurs, stop infusion of KABIVEN immediately and initiate appropriate treatment and supportive measures.

5.5 Precipitation with Ceftriaxone

Precipitation of ceftriaxone-calcium can occur when ceftriaxone is mixed with calcium-containing parenteral nutrition solutions, such as KABIVEN in the same intravenous administration line. Do not administer ceftriaxone simultaneously with KABIVEN via a Y-site. However, in patients other than neonates, ceftriaxone and KABIVEN may be administered sequentially if the infusion lines are thoroughly flushed between infusions with a compatible fluid *[see Dosage and Administration (2.1)]*.

Deaths have occurred in neonates (28 days of age or younger) who received concomitant intravenous calcium-containing solutions with ceftriaxone resulting from calcium-ceftriaxone precipitates in the lungs and kidneys, even when separate infusion lines were used *[see Contraindications (4), Pediatric Use (8.4)]*.

5.6 Infections

Parenteral nutrition, such as KABIVEN, can support microbial growth and is an independent risk factor for the development of catheter-related bloodstream infections. To decrease the risk of infectious complications, ensure aseptic techniques are used for catheter placement, catheter maintenance, and preparation and administration of KABIVEN.

Monitor for signs and symptoms of infection including fever and chills, as well as laboratory test results that might indicate infection (including leukocytosis and hyperglycemia). Perform frequent checks of the intravenous catheter insertion site for edema, redness, and discharge.

5.7 Fat Overload Syndrome

Fat overload syndrome is a rare condition that has been reported with intravenous lipid formulations and is characterized by a sudden deterioration in the patient's condition (e.g., fever, anemia, leukopenia, thrombocytopenia, coagulation disorders, hyperlipidemia, hepatomegaly, deteriorating liver function, and central nervous system manifestations such as coma). A reduced or limited ability

to metabolize lipids, accompanied by prolonged plasma clearance (resulting in higher lipid levels), may result in this syndrome. Although fat overload syndrome has been most frequently observed when the recommended lipid dose or infusion rate was exceeded, cases have also been described when the lipid formulation was administered according to instructions.

If signs or symptoms of fat overload syndrome occur, stop KABIVEN. The syndrome is usually reversible when the infusion including the lipid emulsion is stopped.

5.8 Refeeding Syndrome

Administering PN to severely malnourished patients may result in refeeding syndrome, characterized by the intracellular shift of potassium, phosphorus, and magnesium as patients become anabolic. Thiamine deficiency and fluid retention may also develop. To prevent these complications, closely monitor severely undernourished patients and slowly increase their nutrient intake.

5.9 Diabetes and Hyperglycemia

Administration of dextrose at a rate exceeding the patient's utilization rate may lead to hyperglycemia, hyperosmolar coma, and death. Monitor blood glucose levels and treat hyperglycemia to maintain optimal glucose levels while infusing KABIVEN. Insulin may be administered or adjusted to maintain optimal blood glucose levels during KABIVEN administration.

5.10 Hypertriglyceridemia

The use of KABIVEN is contraindicated in patients with hypertriglyceridemia with serum triglyceride concentrations >1,000 mg/dL.

Patients with conditions such as inherited lipid disorders, obesity, diabetes mellitus, or metabolic syndromes have a higher risk of developing hypertriglyceridemia with the use of KABIVEN. In addition, patients with hypertriglyceridemia may have worsening of their hypertriglyceridemia with administration of KABIVEN. Excessive dextrose administration may further increase such risk. Evaluate patients' capacity to eliminate and metabolize the infused lipid emulsion by measuring serum triglycerides before the start of infusion (baseline value), with each increase in dosage, and regularly throughout treatment. If triglyceride levels are above 400 mg/dL in adults, stop the KABIVEN infusion and monitor serum triglyceride levels to avoid clinical consequences of hypertriglyceridemia such as pancreatitis.

To minimize the risk of new or worsening of hypertriglyceridemia, assess high-risk patients for their overall energy intake including other sources of lipid and dextrose, as well as concomitant drugs that may affect lipid and dextrose metabolism.

5.11 Vein Damage and Thrombosis

The infusion of hypertonic nutrient injections into a peripheral vein may result in vein irritation, vein damage, and/or thrombosis. KABIVEN is only approved for administration into a central vein, such as the superior vena cava *[see Dosage and Administration (2.1)]*. Remove the catheter as soon as possible if thrombophlebitis develops.

5.12 Electrolyte Imbalance and Fluid Overload in Patients with Decreased Renal Function

Patients with decreased renal function, including those with pre-renal azotemia, renal obstruction, or intrinsic renal disease, may be at increased risk of electrolyte and fluid volume imbalance when receiving PN, including KABIVEN. In patients with decreased renal function with electrolyte imbalance or fluid overload, the KABIVEN dosage (e.g., fluid, protein, and electrolyte content) may require adjustment.

Monitor renal function parameters. Patients developing signs of decreased renal function should be assessed early by a clinician knowledgeable in renal disease in order to determine the appropriate KABIVEN dosage.

5.13 Aluminum Toxicity

KABIVEN contains no more than 25 mcg/L of aluminum.

The aluminum contained in KABIVEN may reach toxic levels with prolonged parenteral administration in patients with impaired kidney function. Preterm infants are at greater risk because their kidneys are immature, and they require large amounts of calcium and phosphate solutions that contain aluminum. Patients with impaired kidney function, including preterm infants, 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 of total parenteral nutrition products.

5.14 Monitoring/Laboratory Tests

Monitor fluid status closely in patients with pulmonary edema or heart failure.

Throughout treatment, monitor serum triglycerides *[see Warnings and Precautions (5.13)]*, fluid and electrolyte status, serum osmolarity, blood glucose, liver and kidney function, blood count (including platelets), and coagulation parameters.

KABIVEN contains Vitamin K that may counteract anticoagulant activity *[see Drug Interactions (7)]*.

The lipids contained in KABIVEN may interfere with some laboratory tests (e.g., hemoglobin, triglycerides, lactate dehydrogenase, bilirubin and oxygen saturation) if blood is sampled before the

lipids have cleared from the bloodstream. Conduct these tests at least 6 hours after stopping the infusion.

6 ADVERSE REACTIONS

The following serious adverse reactions are discussed in greater detail in other sections of the prescribing information.

- Clinical Decompensation with Rapid Infusion of Intravenous Lipid Emulsion in Neonates and Infants *[see Warnings and Precautions (5.1)]*.
- Parenteral Nutrition-Associated Liver Disease and Other Hepatobiliary Disorders *[see Warnings and Precautions (5.2)]*.
- Pulmonary Embolism and Respiratory Distress due to Pulmonary Vascular Precipitates *[see Warnings and Precautions (5.3)]*.
- Hypersensitivity Reactions *[see Warnings and Precautions (5.4)]*.
- Precipitation with Ceftriaxone *[see Warnings and Precautions (5.5)]*.
- Infections *[see Warnings and Precautions (5.6)]*.
- Fat Overload Syndrome *[see Warnings and Precautions (5.7)]*.
- Refeeding Syndrome *[see Warnings and Precautions (5.8)]*.
- Diabetes and Hyperglycemia *[see Warnings and Precautions (5.9)]*.
- Hypertriglyceridemia *[see Warnings and Precautions (5.10)]*.
- Vein Damage and Thrombosis *[see Warnings and Precautions (5.11)]*.
- Electrolyte Imbalance and Fluid Overload in Patients with Decreased Renal Function *[see Warnings and Precautions (5.12)]*.
- Aluminum Toxicity *[see Warnings and Precautions (5.13)]*.

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The clinical data described for KABIVEN reflects exposure in 145 patients exposed for 7 days to 4 weeks in 7 active-controlled trials. The pooled population exposed to KABIVEN was 25 to 87 years old, 35% female, 99% Caucasian. The enrolled patients had varied underlying conditions such as gastrointestinal disorders (41%) neoplasms (48%), vascular disorders (35%) and other surgical procedures (21%). Most patients received central intravenous infusion doses of ≥80% of their target mean daily exposure.

Adverse reactions occurring in at least 1% of patients who received KABIVEN are shown in Table 3.

Table 3: Adverse Reactions in >1% of Patients Treated with KABIVEN

Adverse reaction	KABIVEN N=145 (%)
Nausea	22 (15)
Pyrexia	13 (9)
Hypertension	12 (8)
Vomiting	8 (6)
Hemoglobin decreased	8 (6)
Protein total decreased	6 (4)
Hypokalemia	6 (4)
Blood potassium decreased	6 (4)
Gamma-glutamyltransferase increased	6 (4)
Hyperglycemia	3 (2)
Blood alkaline phosphatase increased	2 (1)
Blood calcium decreased	2 (1)
Prothrombin time prolonged	2 (1)
Pruritus	2 (1)
Tachycardia	2 (1)

* Terms as reported in clinical studies

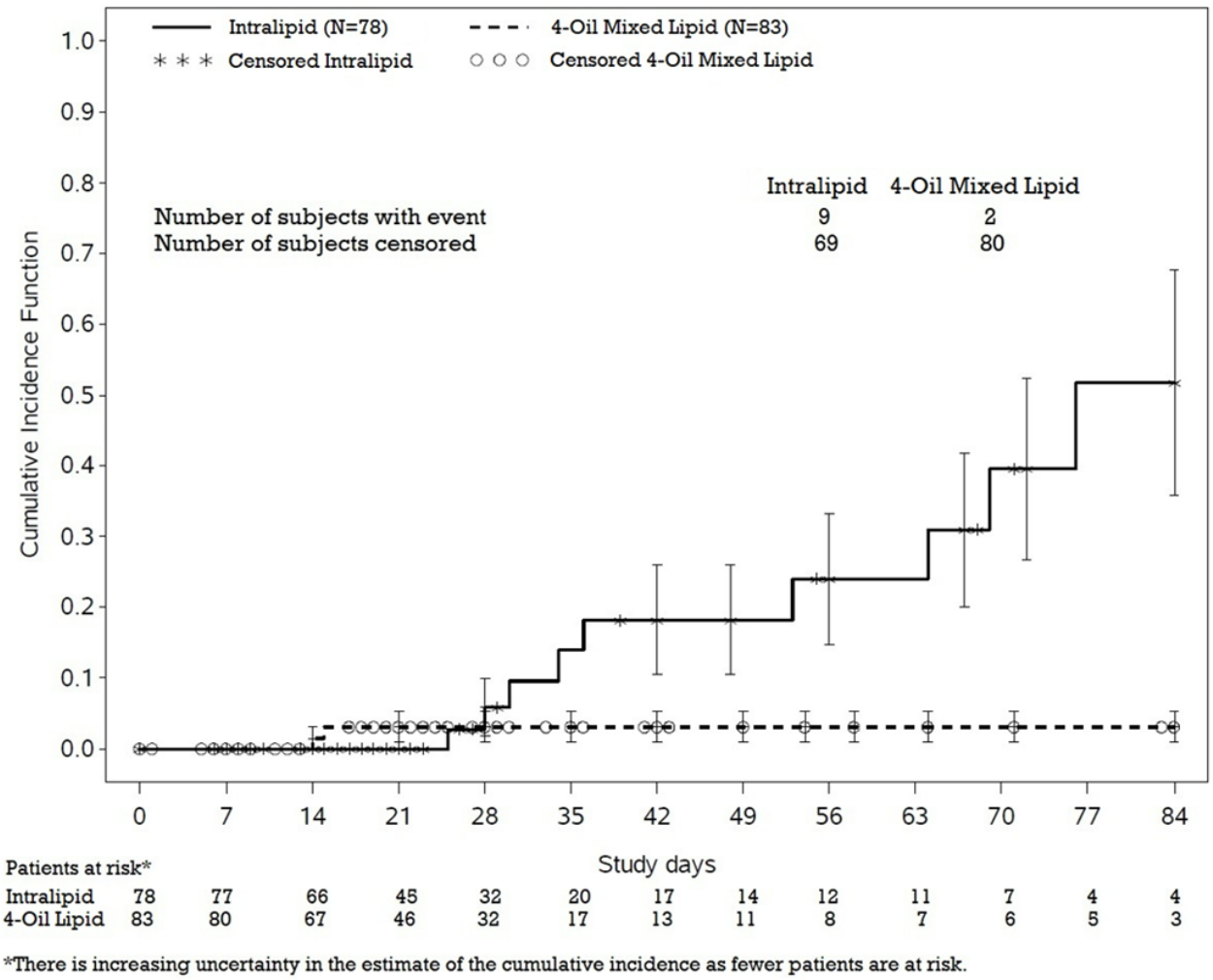
Less common adverse reactions in ≤1% of patients who received KABIVEN were hyperkalemia, hypertriglyceridemia, headache, dizziness, dysgeusia, rash, eczema, blood glucose increased, and increase in blood triglycerides.

In a randomized active-controlled, double-blind, parallel-group, multi-center study that included 152 neonates and 9 patients ranging in age from 29 to 153 days who were expected to require PN for at least 28 days, parenteral nutrition-associated cholestasis (PNAC), a precursor to PNALD, developed more frequently in Intralipid-treated patients than in patients treated with a 4-oil mixed lipid emulsion. Intralipid is the lipid emulsion component of KABIVEN.

PNAC (defined as direct bilirubin >2mg/dl with a second confirmed elevation >2mg/dl at least 7 days later) occurred in 11.5% (9/78) of Intralipid-treated patients and 2.4% (2/83) of patients treated with a 4-oil mixed lipid emulsion. Most PNAC events occurred in patients who were treated for longer than 28 days.

The estimated cumulative incidence of PNAC is shown in the Kaplan-Meier cumulative incidence curve in Figure 1.

Figure 1: Cumulative Incidence Curve of Time to Parenteral Nutrition-Associated Cholestasis (PNAC) with Standard Error Bars



Monitor liver tests in patients treated with KABIVEN and consider discontinuation or dosage reduction if abnormalities occur.

6.2 Postmarketing Experience

The following additional adverse reactions have been identified during post-approval use of KABIVEN in countries where it is registered. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to product exposure.

- Hepatobiliary disorders: cholestasis
- Infections and infestations: infection
- Nervous system disorders: subependymal hemorrhage
- Immune system disorders: hypersensitivity reactions, including anaphylaxis *[see Contraindications (4), Warnings and Precautions (5.4)]*.

7 DRUG INTERACTIONS

7.1 Ceftriaxone

Precipitation of ceftriaxone-calcium can occur when ceftriaxone is mixed with calcium-containing parenteral nutrition solutions, such as KABIVEN, in the same intravenous administration line. Do not administer ceftriaxone simultaneously with KABIVEN via a Y-site. However, ceftriaxone and KABIVEN may be administered sequentially if the infusion lines are thoroughly flushed between infusions with a compatible fluid *[see Dosage and Administration (2.1)]*.

Deaths have occurred in neonates (28 days of age or younger) who received concomitant intravenous calcium-containing solutions with ceftriaxone resulting from calcium-ceftriaxone precipitates in the lungs and kidneys, even when separate infusion lines were used *[see Contraindications (4), Use in Specific Populations (8.4)]*.

7.2 Coumarin and Coumarin Derivatives

The soybean oil present in KABIVEN has vitamin K_1. Vitamin K_1 can reverse the anticoagulant activity of coumarin and coumarin derivatives, including warfarin, which work by blocking recycling of vitamin K_1. Monitor laboratory parameters for anticoagulant activity in patients who are on both KABIVEN and coumarin or coumarin derivatives.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

The limited available data on the use of KABIVEN in pregnant women are not sufficient to inform a drug-associated risk. However, there are clinical considerations if KABIVEN is used in pregnant women *[see Clinical Considerations]*. Animal reproduction studies have not been conducted with KABIVEN.

The estimated background risk of major birth defects and miscarriage for the indicated population are unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

Clinical Considerations

Disease-Associated Maternal and/or Embryofetal Risk

Severe malnutrition in a pregnant woman is associated with preterm delivery, low birth weight, intrauterine growth restriction, congenital malformations and perinatal mortality. Parenteral nutrition should be considered if a pregnant woman's nutritional requirements cannot be fulfilled by oral or enteral intake.

8.2 Lactation

Risk Summary

There are no data available to assess the presence of KABIVEN and/or its active metabolite(s) in human milk, the effects on the breastfed child or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for KABIVEN, and any potential adverse effects of KABIVEN on the breastfed child or from the underlying maternal condition.

8.4 Pediatric Use

The safety and effectiveness of KABIVEN has not been established in pediatric patients of any age.

In the postmarketing setting, clinical decompensation with rapid infusion of intravenous lipid emulsion in neonates and infants, sometimes fatal has been reported *[see Warnings and Precautions (5.1)]*. Patients, particularly preterm infants, are at risk for aluminum toxicity *[see Warnings and Precautions (5.13)]*.

Deaths have occurred in neonates (28 days of age or younger) who received concomitant intravenous calcium-containing solutions with ceftriaxone resulting from calcium-ceftriaxone precipitates in the lungs and kidneys, even when separate infusion lines were used. *[see Contraindications (4), Warnings and Precautions (5.5)]*.

KABIVEN is not recommended for use in pediatric patients under the age of two years, including preterm infants, as the fixed content of the formulation does not meet the nutritional requirements of this age group due to the following reasons:

1. Calcium and dextrose needs are not met and lipids, protein and magnesium exceed requirements.
2. The product does not contain the amino acids cysteine and taurine, considered conditionally essential for neonates and infants.

Patients, including pediatric patients, may be at risk for PNALD *[see Warnings and Precautions (5.2)]*.

Newborns – especially those born premature and with low birth weight – are at increased risk of developing hypo – or hyperglycemia and therefore need close monitoring during treatment with intravenous dextrose solutions to ensure adequate glycemic control in order to avoid potential long term adverse effects. Hypoglycemia in the newborn can cause prolonged seizures, coma and brain damage. Hyperglycemia has been associated with intraventricular hemorrhage, late onset bacterial and fungal infection, retinopathy of prematurity, necrotizing enterocolitis, bronchopulmonary dysplasia, prolonged length of hospital stay, and death.

8.5 Geriatric Use

Clinical studies of KABIVEN did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently from other younger patients. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or drug therapy.

10 OVERDOSAGE

In the event of overdose, serious adverse reactions may result *[see Warnings and Precautions (5.1, 5.7)]*. Stop the infusion of KABIVEN to allow lipids to clear from serum. The effects are usually reversible after the lipid infusion is stopped. If medically appropriate, further intervention may be indicated. The lipid administered and fatty acids produced are not dialyzable.

11 DESCRIPTION

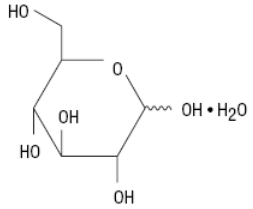
KABIVEN is a sterile, hypertonic emulsion, for central venous administration, in a Three Chamber Bag. The product contains no added sulfites.

Chamber 1 contains Dextrose monohydrate solution for fluid replenishment and caloric supply.

Chamber 2 contains the Amino Acid solution with Electrolytes, which comprises essential and nonessential amino acids provided with electrolytes.

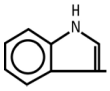
Chamber 3 contains Intralipid® 20% (a 20% Lipid Injectable Emulsion), prepared for intravenous administration as a source of calories and essential fatty acids.
See below for formulations of each chamber and Table 2 for strength, pH, osmolarity, ionic concentration and caloric content of KABIVEN when all the chambers are mixed together.

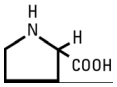
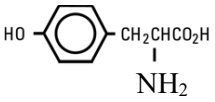
Chamber 1: Contains sterile, hypertonic solution of Dextrose, USP in water for injection with a pH range of 3.5 to 5.5. Dextrose, USP is chemically designated D-glucose, monohydrate ($C_6H_{12}O_6 \cdot H_2O$) and has the following structure:



Dextrose is derived from corn.

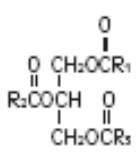
Chamber 2: Contains a sterile, solution of amino acids and electrolytes in water for injection. In addition, glacial acetic acid has been added to adjust the pH so that the final solution pH is 5.4 to 5.8. The formulas for the individual electrolytes and amino acids are as follows:

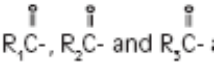
Electrolytes	
Sodium Acetate Trihydrate, USP	$CH_3COONax3H_2O$
Potassium Chloride, USP	KCl
Sodium Glycerophosphate	$C_3H_5(OH)_2PO_4Na_2xH_2O$
Magnesium Sulfate Heptahydrate, USP	$MgSO_4x7H_2O$
Calcium Chloride Dihydrate, USP	$CaCl_2x2H_2O$
Essential Amino Acids	
Lysine (added as the hydrochloride salt)	$H_2N(CH_2)_4CH(NH_2)COOH.HCl$
Phenylalanine	 $CH_2CH(NH_2)COOH$
Leucine	$(CH_3)_2CHCH_2CH(NH_2)COOH$
Valine	$(CH_3)_2CHCH(NH_2)COOH$
Histidine	 CH2CH(NH2)COOH
Threonine	$CH_3CH(OH)CH(NH_2)COOH$
Methionine	$CH_3S(CH_2)_2CH(NH_2)COOH$
Isoleucine	$CH_3CH_2CH(CH_3)CH(NH_2)COOH$
Tryptophan	 $CH_2CH(NH_2)COOH$
Nonessential Amino Acids	
Alanine	$CH_3CH(NH_2)COOH$

Arginine	$H_2NC(NH)NH(CH_2)_3CH(NH_2)COOH$
Glycine	H_2NCH_2COOH
Proline	
Glutamic Acid	$HOOC(CH_2)_2CH(NH_2)COOH$
Serine	$HOCH_2CH(NH_2)COOH$
Aspartic Acid	$HOOCCH_2CH(NH_2)COOH$
Tyrosine	

Chamber 3: Contains a 20% Lipid Injectable Emulsion (Intralipid® 20%) which is made up of 20% Soybean Oil, 1.2% Egg Yolk Phospholipids, 2.25% Glycerin, and water for injection. In addition, sodium hydroxide has been added to adjust the pH. The final product pH range is 6 to 9.

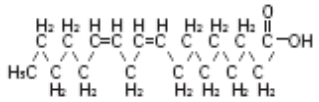
The soybean oil is a refined natural product consisting of a mixture of neutral triglycerides of predominantly unsaturated fatty acids with the following structure:



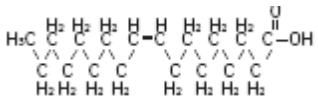
where  are saturated and unsaturated fatty acid residues. The major component fatty acids are linoleic (48 to 58 %), oleic (17 to 30%), palmitic (9 to 13%), linolenic (5 to 11%) and stearic acid (2.5 to 5%).

These fatty acids have the following chemical and structural formulas:

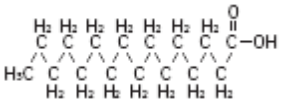
Linoleic acid
$C_{18}H_{32}O_2$



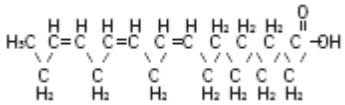
Oleic acid
$C_{18}H_{34}O_2$



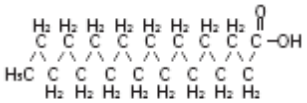
Palmitic acid
$C_{16}H_{32}O_2$



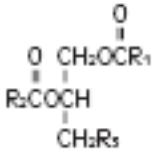
Linolenic acid
$C_{18}H_{30}O_2$

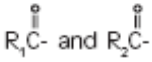


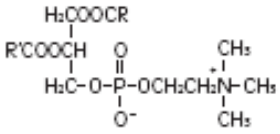
Stearic acid
$C_{18}H_{36}O_2$



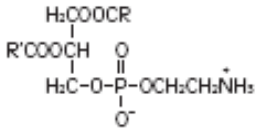
Purified egg phosphatides are a mixture of naturally occurring phospholipids which are isolated from the egg yolk. These phospholipids have the following general structure:



 contain saturated and unsaturated fatty acids that abound in neutral fats. R3 is primarily either the choline or ethanolamine ester of phosphoric acid.

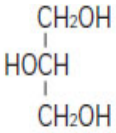


Phosphatidylcholine



Phosphatidylethanolamine

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



The container-solution 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 oxygen and moisture barrier when necessary. An oxygen absorber is placed between the inner bag and the overpouch.

The container is not made with natural rubber latex or polyvinyl chloride (PVC).

KABIVEN contains no more than 25 mcg/L of aluminum.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

KABIVEN is used as a supplement or as the sole source of nutrition in patients, providing macronutrients (amino acids, dextrose and lipids) and micronutrients (electrolytes) parenterally.

The amino acids provide the structural units that make up proteins and are used to synthesize proteins and other biomolecules or are oxidized to urea and carbon dioxide as a source of energy.

The administered dextrose is oxidized to carbon dioxide and water, yielding energy.

Intravenously administered lipids provide a biologically utilizable source of calories and essential fatty acids. Fatty acids serve as an important substrate for energy production. The most common mechanism of action for energy derived from fatty acid metabolism is beta- oxidation. Fatty acids are important for membrane structure and function, precursors for bioactive molecules (such as prostaglandins), and as regulators of gene expression.

12.3 Pharmacokinetics

The infused lipid particles provided by KABIVEN are expected to be cleared from the blood stream in a manner thought to be comparable to the clearing of chylomicrons. In healthy volunteers, the maximum clearance rate of the triglycerides after fasting overnight has been found to be 3.8 ± 1.5 g/kg per 24 hours. Both elimination and oxidation rates are dependent on the patient's clinical condition; elimination is faster and utilization is increased in postoperative patients, in sepsis, burns and trauma, while patients with renal impairment and hypertriglyceridemia may show lower utilization of exogenous lipid emulsions. Due to differences in elimination, patients with these conditions should be closely monitored during KABIVEN administration *[see Warnings and Precautions (5.12, 5.13)]*.

The disposition of infused amino acids, dextrose and electrolytes are essentially the same as those supplied by ordinary food.

A clinical study in healthy volunteers employing high intravenous doses (80 mmol) of either sodium glycerophosphate used in KABIVEN or reference, inorganic sodium phosphate demonstrated that both compounds resulted in comparable serum inorganic phosphate concentrations after a single intravenous dose. Changes from baseline in the serum levels of sodium, potassium and total calcium were comparable across the two phosphate sources in this study.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term animal studies have not been conducted to evaluate carcinogenic potential of KABIVEN or its effect on fertility. Genotoxicity studies have not been conducted with KABIVEN to assess its mutagenic potential.

16 HOW SUPPLIED/STORAGE AND HANDLING

KABIVEN is a sterile emulsion available in the following 4 sizes:

NDC	Volume
63323-712-25	2,566 mL
63323-712-20	2,053 mL
63323-712-15	1,540 mL
63323-712-10	1,026 mL

Exposure of pharmaceutical products to heat should be minimized. Avoid excessive heat. Protect from freezing. If accidentally frozen, discard the bag. It is recommended that the product be stored at 5°C to 25°C (41°F to 77°F).

Do not remove container from overpouch until intended for use.

After breaking the vertical seals, chemical and physical in-use stability of the mixed three chamber bag has been demonstrated for 48 hours at 25°C (77°F). If not used immediately, the activated bag can be stored for up to 7 days under refrigeration [2° to 8°C (36º to 46°F)]. After removal from refrigeration, the activated bag should be used within 48 hours.

The product should be used immediately after the introduction of additives. If not used immediately, the storage time and conditions prior to use should not be longer than 24 hours at 2° to 8°C (36° to 46°F). After removal from storage at 2° to 8°C (36° to 46°F), the admixture should be infused within 24 hours. Any mixture remaining must be discarded.

17 PATIENT COUNSELING INFORMATION

When initiating KABIVEN administration, discuss the following information with the patient or caregiver:

Parenteral Nutrition-Associated Liver Disease and Other Hepatobiliary Disorders

Inform patients and caregivers that use of parenteral nutrition may result in parenteral nutrition-associated liver disease and/or other hepatobiliary disorders *[see Warnings and Precautions (5.2)]*.

Pulmonary Embolism and Respiratory Distress due to Pulmonary Vascular Precipitates

Inform patients and caregivers that pulmonary vascular precipitates causing pulmonary emboli (including some fatalities) and presenting as respiratory distress have been reported in patients receiving parenteral nutrition. If KABIVEN is infused at home, instruct patients or caregivers to visually inspect the prepared solution, the infusion set, and catheter for precipitates, prior to administration as well as periodically during the administration *[see Warnings and Precautions (5.3)]*.

Hypersensitivity Reactions

Inform patients and caregivers that KABIVEN may cause hypersensitivity reactions, including anaphylaxis. If KABIVEN is infused at home, instruct patients or caregivers to stop the infusion of KABIVEN immediately and seek medical attention if they experience signs or symptoms of a hypersensitivity reaction, such as rapid or weak heartbeat, feeling faint, difficulty in breathing or swallowing, vomiting, nausea, headache, sweating, dizziness, hives, rash, itching, flushing, dizziness, fever, or chills *[see Warnings and Precautions (5.4)]*.

Infections

Inform patients and caregivers that patients who receive KABIVEN are at risk of infection. If KABIVEN is infused at home, instruct patients or caregivers to ensure aseptic techniques are used for the preparation and administration of KABIVEN and to monitor for signs and symptoms of infection *[see Warnings and Precautions (5.6)]*.

Fat Overload Syndrome

Inform patients and caregivers that fat overload syndrome has been reported with the use of intravenous lipid emulsions. If KABIVEN is infused at home, instruct patients or caregivers to stop KABIVEN if signs or symptoms of fat overload syndrome occur *[see Warnings and Precautions (5.7)]*.

Refeeding Syndrome

If the patient is severely malnourished, inform patients and caregivers that administering parenteral nutrition including KABIVEN may result in refeeding syndrome *[see Warnings and Precautions (5.8)]*.

Diabetes and Hyperglycemia

Inform patients and caregivers that administration of dextrose at a rate exceeding the patient's utilization rate may lead to hyperglycemia, hyperosmolar coma, and death [*see Warnings and Precautions (5.9).*

Hypertriglyceridemia

Inform patients and caregivers about the risks of hypertriglyceridemia with KABIVEN use *[see Warnings and Precautions (5.10)]*.

Electrolyte Imbalance and Fluid Overload in Patients with Decreased Renal Function

For patients with decreased renal function, inform them or their caregivers that the patient may be at increased risk of electrolyte and fluid volume imbalance when KABIVEN is being administered *[see Warnings and Precautions (5.12)]*.

Aluminum Toxicity

Inform patients and caregivers that prolonged PN administration in patients with renal impairment, including preterm neonates, may result in aluminum reaching toxic levels associated with central nervous system and bone toxicity *[see Warnings and Precautions (5.13)].*

Preparation and Administration Instructions

If it is acceptable for a patient or caregiver to administer KABIVEN at home, then the patient or caregiver must be trained on the following: how to inspect and prepare, add compatible additives (when appropriate), administer, and store KABIVEN *[see Dosage and Administration (2.1, 2.2, 2.3)].* Inform patients or caregivers not to deviate from the administration instructions given by the healthcare provider.

Manufactured by:

FRESENIUS KABI
Uppsala, Sweden

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www.freseniuskabinutrition.com/products/kabiven-perikabiven/

Package Insert Part Number Pending