FRESENIUS KABI
caring for life

Fresenius Kabi USA **Nutrition**

As a global innovator in clinical nutrition, we create innovations that nourish

Explore the full portfolio of lipid injectable emulsions (ILEs) for parenteral nutrition (PN) from the U.S. market leader in ILEs.[1]

FRIEND OF THE SEA

We're proud to support marine conservation by ensuring that the fish oil in our products is sustainably sourced.

Omegaven®

(fish oil triglycerides) injectable emulsion

A **first in PN** from the **leaders in PN**

Omegaven is the **FIRST** and **ONLY 100% fish oil ILE** for pediatric patients with parenteral nutrition-associated cholestasis (PNAC) in the U.S.[2]

- Omegaven is a source of calories and fatty acids for pediatric patients with PNAC[2]
- Patients receiving Omegaven achieved age-appropriate growth[2]
- Omegaven-treated patients experienced improvement in liver function parameters[2]
  - During clinical trials, 113 out of 189 of Omegaven-treated patients reached direct bilirubin (DBIL) levels <2 mg/dL and aspartate aminotransferase (AST) or alanine aminotransferase (ALT) levels <3 times the upper limit of normal at end of study[2]

Patients in our clinical trials conducted at Boston Children's Hospital and Texas Children's Hospital received Omegaven for a median of 2.7 months and up to 8 years.[2]

ESPGHAN/ESPEN/ESPR/CSPEN guidelines for pediatric patients[3]:

"In pediatric patients, intravenous lipid emulsions (ILEs) should be an integral part of parenteral nutrition (PN) either exclusive or complementary to enteral feeding (LoE 1-, RG A, strong recommendation for)."

Omegaven is indicated as a source of calories and fatty acids in pediatric patients with parenteral nutrition-associated cholestasis (PNAC). **Limitations of Use:** Omegaven is not indicated for the prevention of PNAC. It has not been demonstrated that Omegaven prevents PNAC in parenteral nutrition (PN)-dependent patients. It has not been demonstrated that the clinical outcomes observed in patients treated with Omegaven are a result of the omega-6: omega-3 fatty acid ratio of the product. **Contraindications:** Omegaven is contraindicated in patients with known hypersensitivity to fish or egg protein or to any of the active ingredients or excipients, severe hemorrhagic disorders due to a potential effect on platelet aggregation, severe hyperlipidemia or severe disorders of lipid metabolism characterized by hypertriglyceridemia (serum triglyceride concentrations greater than 1,000 mg/dL).

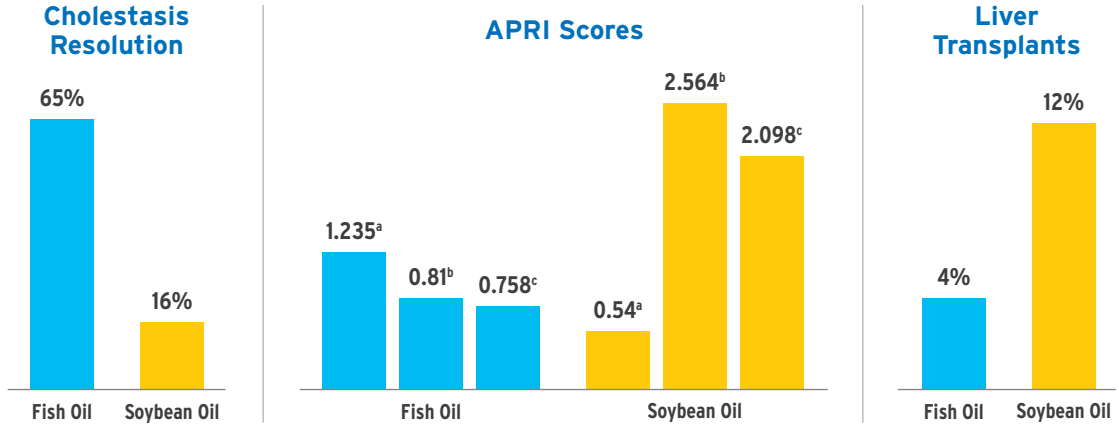
Please see Brief Summary of Prescribing Information for Omegaven on pages 12-13.

Omegaven demonstrated reduced liver parameters and reduced transplantation in patients with PNAC

Study design[4]

In this multicenter integrated analysis, fish oil-based lipid emulsions (FOLE) recipients (1 g/kg/d) (n = 189) were compared with historical controls administered soybean oil-based lipid emulsion (SOLE) (<3 g/kg/d) (n = 73). Patients were <2 years of age with direct bilirubin ≥2 mg/dL. They were also expected to require PN for 30 days or more and had failed to respond to standard therapies for intestinal failure-associated liver disease (IFALD).

Results[4]



[a]Baseline, [b]Cholestasis Resolution, [c]End of Study

FOLE recipients experienced a higher rate of cholestasis resolution (*P*<.0001), lower aspartate aminotransferase to platelet ratio index (APRI; *P*<.02 vs *P*<.0003, respectively), and fewer liver transplants (*P*<.0245) compared with SOLE. This study demonstrates that a fish oil ILE may be preferred in children with IFALD when direct or conjugated bilirubin reaches 2 mg/dL.[4]

ORDERING INFORMATION		
Bottle Size	50 mL single-dose glass bottle	100 mL single-dose glass bottle
NDC Code	63323-205-50	63323-205-00
Bottles/Carton	10 bottles/carton	10 bottles/carton

Please see Brief Summary of Prescribing Information for Omegaven on pages 12-13.

SMOFlipid®
Lipid Injectable Emulsion, USP 20%

Discover the SMOF **difference**

SMOFlipid is a unique blend of 4 oil sources[5]

Soybean oil 30%
(omega-6)
Provides essential fatty acids.

Medium-chain triglycerides (MCT) 30%
A source of rapidly available energy.[6]

Olive oil 25%
(omega-9) Supplies monounsaturated fatty acids.

Fish oil 15%
(omega-3) A source of EPA and DHA.[7]

SMOFlipid is indicated in adult and pediatric patients, including term and preterm neonates, as a source of calories and essential fatty acids for PN when oral or enteral nutrition is not possible, insufficient, or contraindicated.

Contraindications: Known hypersensitivity to fish, egg, soybean, or peanut, or to any of the active or inactive ingredients in SMOFlipid. Severe disorders of lipid metabolism characterized by hypertriglyceridemia (serum triglycerides > 1,000 mg/dL).

Please see Brief Summary of Prescribing Information for SMOFlipid on pages 14-15.

This **unique 4-oil blend** aligns with recommended plasma ratios

Lipid Emulsion	Ratio of Omega-6:Omega-3 Fatty Acids
Recommendations[8-11]	2:1 to 4:1
Soybean-Oil Emulsion	7:1
MCT/LCT Emulsion	7:1
Olive Oil/Soybean-Oil Emulsion	9:1
SMOFlipid[5]	2.5:1

MCT=medium-chain triglyceride; LCT=long-chain triglyceride

- Patients receiving soybean oil-based lipid emulsions may be exposed to high levels of omega-6 polyunsaturated fatty acids and a virtual absence of omega-3 fatty acids[8]

The **SMOF** Difference

In adults

- SMOFlipid has been shown to improve EPA and DHA in adult patients compared to those receiving a soybean oil-based lipid emulsion*[11,12]

In pediatrics

- The safety and efficacy of SMOFlipid compared to soybean oil in pediatric patients of all groups, including term and preterm neonates, was evaluated in 333 pediatric patients in four randomized, active-controlled, double-blind, parallel-group controlled clinical studies[5]
- SMOFlipid is safe and well tolerated in preterm neonates, infants, and children[13-15]
- Preterm infants receiving SMOFlipid experienced higher EPA and DHA levels compared to those receiving a soybean oil lipid emulsion*[13,16]

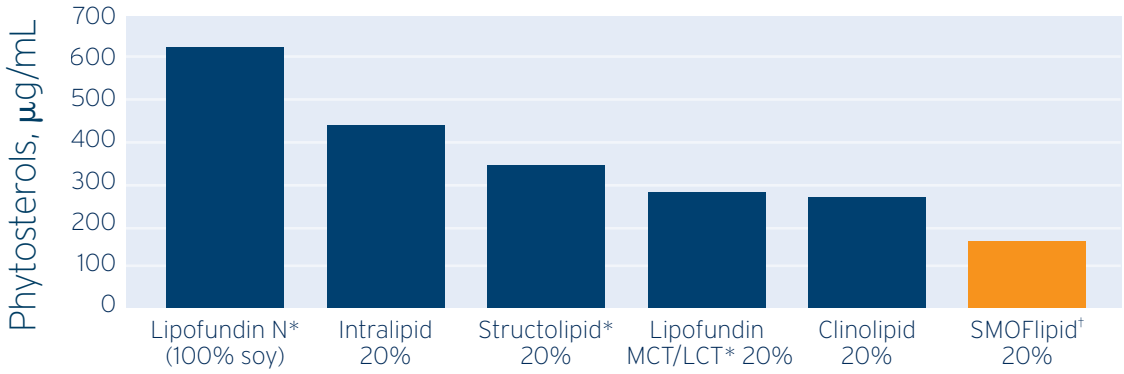
*Based on composition of the product.

EPA and DHA

- ESPEN states, "Addition of EPA and DHA to lipid emulsions has demonstrable effects on cell membranes and inflammatory processes (Grade B)"[17]

Phytosterols in PN

ILEs and Phytosterol Content



Xu Z, et al. *Nutrients*. 2012;4:904-921.[18]
*Not approved in the U.S.
†Data on file.

The predominant phytosterol in these emulsions was beta-sitosterol, the major phytosterol in plant oils (e.g., soybean oil, olive oil, sunflower oil, etc.).

Per milliliter, **SMOFlipid contains the lowest amount of phytosterols in commercially available ILEs** indicated for adults[18,19]

Give your patients the one and only SMOF

- Meets the essential fatty acid requirements for PN patients of all ages[5]
- Contains fish oil, which is rich in omega-3s
- Demonstrated safety and tolerability[12,20]
- More than 7 million patients globally received SMOFlipid‡

‡Data on file.

SMOFlipid resulted in a lower incidence of parenteral nutrition-associated cholestasis (PNAC)*

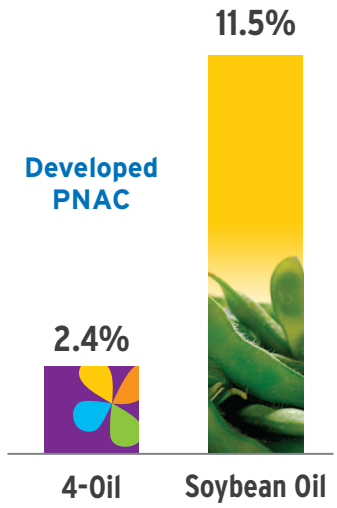
Study design

The hepatic safety of SMOFlipid was evaluated 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.[5]

Results

PNAC mostly occurred in patients who received treatment for more than 28 days.[5]

**There is increasing uncertainty in the estimate of the cumulative incidence as fewer patients are at risk over the course of 84 days.*



ORDERING INFORMATION				
Bag Size	100 mL	250 mL	500 mL	1000 mL
NDC Code	63323-820-00	63323-820-74	63323-820-50	63323-820-10
Bags/Case	10 bags/case	10 bags/case	12 bags/case	6 bags/case

Kabiven®
(Amino Acids, Electrolytes, Dextrose, and Lipid Injectable Emulsion), for intravenous use

Perikabiven®
(Amino Acids, Electrolytes, Dextrose, and Lipid Injectable Emulsion), for intravenous use

Drive standardization with the **FIRST** and **ONLY three-chamber bag** for PN in the U.S.

The Kabiven and Perikabiven three-chamber PN bags efficiently deliver three macronutrients (dextrose, protein, and lipids) plus electrolytes in volumes and concentrations that meet the needs of most PN patients.[21,22]

Standardization with a three-chamber bag can:

- Limit the risk of contamination that may be introduced by traditional compounding[23]
- Minimize errors associated with ordering, transcription, and compounding[24]
- Eliminate the need to piggyback lipids
- Be dispensed by pharmacy anytime, including nights and weekends
- Be a source of electrolytes, such as magnesium sulfate and sodium glycerophosphate, during drug shortages

An all-in-one solution in a three-chamber bag can **simplify**:

- Calculations for dietitians
- Compounding for pharmacists
- Prescription writing for clinicians
- Administration for nurses

 Please see Brief Summary of Prescribing Information for Kabiven and Perikabiven on pages 16-17.

Evaluating **time**, **labor**, and **cost savings**

In a multicenter, prospective, time and motion study evaluating PN delivery systems, Kabiven (representing 3CB delivery systems) was associated with a 62% reduction in pharmacy staff time and workload as well as a 37% reduction in costs compared with hospital-compounded bags (representing PN prepared with automated compounding devices).[25]

Kabiven was associated with a **62% reduction** in pharmacy staff time[25]

Kabiven was associated with a **37% reduction** in costs[25]

ORDERING INFORMATION

	Kabiven (central PN)				Perikabiven (peripheral or central PN)	
Volume	1026 mL	1540 mL	2053 mL	2566 mL	1440 mL	1920 mL
NDC Code	63323-712-10	63323-712-15	63323-712-20	63323-712-25	63323-714-14	63323-714-19
Number of Bags per Case	4 bags/case	4 bags/case	4 bags/case	3 bags/case	4 bags/case	4 bags/case

KABIVEN and PERIKABIVEN are each 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 and PERIKABIVEN may be used to prevent essential fatty acid deficiency or treat negative nitrogen balance in adult patients.

Limitations of Use

Neither KABIVEN nor PERIKABIVEN are 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.

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

Intralipid®
(lipid injectable emulsion, USP 20%)

A long-standing and **trusted lipid** choice worldwide

- FDA approved for over 40 years
- 100% soybean oil
- Well documented in medical literature
- Provided in more than 200 million infusions* for adult and pediatric patients
- Effective source of calories and essential fatty acids[26]

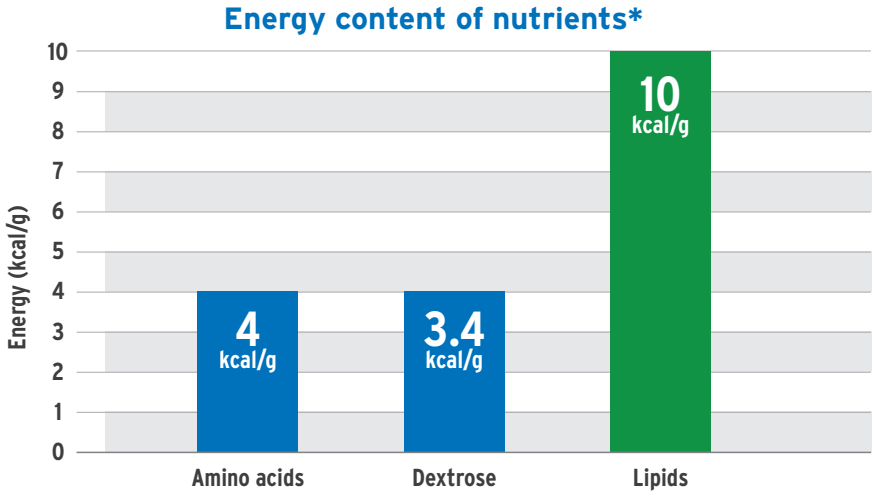
*Data on file.

Intralipid 20% composition

Content per 1L	Intralipid 20%
Soybean oil (g)	200
Osmolality (mOsm/kg water)	350
Inorganic phosphate (mmol)	15
Total caloric value (kcal/mL)	2

Lipids are an efficient energy source

Compared with other PN macronutrients, lipids are the most calorically dense and can be the most beneficial for volume-restricted patients



*Standard values published in the Codex Alimentarius by United Nations' Food Agriculture Organisation (FAO).

Please see Brief Summary of Prescribing Information for Intralipid on pages 18-19.

Intralipid has been used in a **wide range** of patient types

- Critically ill patients e.g. with trauma, burns, sepsis, and SIRS†
- Surgical patients
- Patients with gastrointestinal tract cancer
- Patients with renal insufficiency
- Pediatric patients
- Patients on Home Parenteral Nutrition (HPN)

†SIRS = Systemic Inflammatory Response Syndrome

This chart represents a non-exhaustive list of patient populations who have been prescribed Intralipid. This chart is provided for informational purposes and is not intended to influence or act as a substitute for a healthcare professional's independent medical judgment.

ORDERING INFORMATION

Bag Size and Concentration	100 mL 20%	250 mL 20%	500 mL 20%	1000 mL 20%	500 mL 30%
NDC Code	65219-531-10	65219-533-25	65219-535-50	65219-539-10	65219-537-50
Bags/Case	10 bags/case	10 bags/case	12 bags/case	6 bags/case	12 bags/case

Intralipid 20% (A 20% Intravenous Fat Emulsion), is indicated as a source of calories and essential fatty acids for patients requiring parenteral nutrition (PN) and as a source of essential fatty acids for prevention of essential fatty acid deficiency (EFAD).

Intralipid 20% Pharmacy Bulk Package and Intralipid 30% Pharmacy Bulk Package are intended for use in a pharmacy admixture program for the preparation of three-in-one or total nutrition admixtures (TNAs) to provide a source of calories and essential fatty acids for adult and pediatric patients requiring PN and a source of essential fatty acids for prevention of EFAD.

INTRALIPID 20% and 30% PHARMACY BULK PACKAGES ARE NOT INTENDED FOR DIRECT INTRAVENOUS ADMINISTRATION.

Contraindications: Known hypersensitivity to egg, soybean, or peanut, or any of the active ingredients or excipients. Severe disorders of lipid metabolism characterized by hypertriglyceridemia (serum triglyceride > 1,000 mg/dL). Disturbances of normal fat metabolism such as pathologic hyperlipemia, lipoid nephrosis or acute pancreatitis if accompanied by hyperlipidemia.

Please see Brief Summary of Prescribing Information for Intralipid on pages 18-19.

OMEGAVEN (fish oil triglycerides) injectable emulsion, for intravenous use

BRIEF SUMMARY OF PRESCRIBING INFORMATION

This brief summary does not include all the information needed to use Omegaven safely and effectively. Please see full prescribing information for Omegaven (fish oil triglycerides) injectable emulsion for intravenous use at www.FreseniusKabiNutrition.com/OmegavenPI.

INDICATIONS AND USAGE

Omegaven is indicated as a source of calories and fatty acids in pediatric patients with parenteral nutrition-associated cholestasis (PNAC).

Limitations of Use

Omegaven is not indicated for the prevention of PNAC. It has not been demonstrated that Omegaven prevents PNAC in parenteral nutrition (PN)-dependent patients.

It has not been demonstrated that the clinical outcomes observed in patients treated with Omegaven are a result of the omega-6: omega-3 fatty acid ratio of the product.

DOSAGE AND ADMINISTRATION

Protect the admixed PN solution from light. Prior to administration, correct severe fluid and electrolyte disorders and measure serum triglycerides to establish a baseline level. Initiate dosing in PN-dependent pediatric patients as soon as direct or conjugated bilirubin levels are 2 mg/dL or greater. The recommended nutritional requirements of fat and recommended dosage of Omegaven to meet those requirements for pediatric patients are provided in Table 1, along with recommendations for the initial and maximum infusion rates. Do not exceed the maximum infusion rate in Table 1. Administer Omegaven until direct or conjugated bilirubin levels are less than 2 mg/dL or until the patient no longer requires PN. Use a 1.2 micron in-line filter during administration.

Table 1: Recommended Pediatric Dosage and Infusion Rate

Nutritional Requirements	Direct Infusion Rate	
Recommended Initial Dosage and Maximum Dosage	Initial	Maximum
1 g/kg/day; this is also the maximum daily dose	0.2 mL/kg/hour for the first 15 to 30 minutes; gradually increase to the required rate after 30 minutes	1.5 mL/kg/hour

CONTRAINDICATIONS

Omegaven is contraindicated in patients with known hypersensitivity to fish or egg protein or to any of the active ingredients or excipients, severe hemorrhagic disorders due to a potential effect on platelet aggregation, severe disorders of lipid metabolism characterized by hypertriglyceridemia (serum triglyceride concentrations greater than 1,000 mg/dL).

WARNINGS AND PRECAUTIONS

- Clinical Decompensation with Rapid Infusion of Lipid Injectable Emulsions in Neonates and Infants In the postmarket setting, serious adverse reactions including acute respiratory distress, metabolic acidosis, and death have been reported in neonates and infants after rapid infusion of lipid injectable emulsions. Hypertriglyceridemia was commonly reported. Strictly adhere to the recommended total daily dosage; the hourly infusion rate should not exceed 1.5 mL/kg/hour. Preterm and small for gestational age infants have poor clearance of lipid injectable emulsions and increased free fatty acid plasma levels following 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 of poor clearance of lipids from the circulation occur, stop the infusion and initiate a medical evaluation.
- Hypersensitivity Reactions: Omegaven contains fish oil and egg phospholipids, which may cause hypersensitivity reactions. Signs or symptoms of a hypersensitivity reaction may include: tachypnea, dyspnea, hypoxia, bronchospasm, tachycardia, hypotension, cyanosis, vomiting, nausea, headache, sweating, dizziness, altered mentation, flushing, rash, urticaria, erythema, fever, or chills. If a hypersensitivity reaction occurs, stop infusion of Omegaven immediately and initiate appropriate treatment and supportive measures.
- Infections: The risk of infection is increased in patients with malnutrition-associated immunosuppression, long-term use and poor maintenance of intravenous catheters, or immunosuppressive effects of other conditions or concomitant drugs. To decrease the risk of infectious complications, ensure aseptic technique in catheter placement and maintenance, as well as in the preparation and administration of Omegaven. Monitor for signs and symptoms of early infections including fever and chills, laboratory test results that might indicate infection (including leukocytosis and hyperglycemia), and frequently inspect the intravenous catheter insertion site for edema, redness, and discharge
- Fat Overload Syndrome: A reduced or limited ability to metabolize lipids accompanied by prolonged plasma clearance may result in this syndrome, which is characterized by a sudden deterioration in the patient's condition including fever, anemia, leukopenia, thrombocytopenia, coagulation disorders, hyperlipidemia, hepatomegaly, deteriorating liver function, and central nervous system manifestations (e.g., coma).
- 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 the patient becomes anabolic. Thiamine deficiency and fluid retention may also develop. To prevent these complications, closely monitor severely malnourished patients and slowly increase their nutrient intake.
- Hypertriglyceridemia: Impaired lipid metabolism with hypertriglyceridemia may occur in conditions such as inherited lipid disorders, obesity, diabetes mellitus, and metabolic syndrome. Serum triglyceride levels greater than 1,000 mg/dL have been associated with an increased risk of pancreatitis. To evaluate the patient's capacity to metabolize and eliminate the infused lipid emulsion, measure serum triglycerides before the start of infusion (baseline value), and regularly throughout treatment. If hypertriglyceridemia (triglycerides greater than 250 mg/dL in neonates and infants or greater than 400 mg/dL in older children) develops, consider stopping the administration of Omegaven for 4 hours and obtain a repeat serum triglyceride level. Resume Omegaven based on new result as indicated.
- Aluminum Toxicity: Omegaven contains no more than 25 mcg/L of aluminum. Aluminum may reach toxic levels with prolonged parenteral administration if kidney function is impaired.

Preterm infants are particularly at risk because their kidneys are immature, and they require large amounts of calcium and phosphate solutions, which 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.

- Monitoring and Laboratory Tests: Routine Monitoring: Monitor serum triglycerides, fluid and electrolyte status, serum osmolarity, blood glucose, liver and kidney function, coagulation parameters, and complete blood count including platelets throughout treatment. Essential Fatty Acids: Monitoring patients for laboratory evidence of essential fatty acid deficiency (EFAD) is recommended. Laboratory tests are available to determine serum fatty acids levels. Reference values should be consulted to help determine adequacy of essential fatty acid status
- Interference with Laboratory Tests: The lipids contained in Omegaven may interfere with some laboratory blood tests (e.g., hemoglobin, lactate dehydrogenase, bilirubin, and oxygen saturation) if blood is sampled before lipids have cleared from the bloodstream. Lipids are normally cleared after a period of 5 to 6 hours once the lipid infusion is stopped.

ADVERSE REACTIONS

The most common adverse drug reactions (>15%) are: vomiting, agitation, bradycardia, apnea and viral infection.

Clinical Trials Experience

The safety database for Omegaven reflects exposure in 189 pediatric patients (19 days to 15 years of age) treated for a median of 14 weeks (3 days to 8 years) in two clinical trials.

Adverse reactions that occurred in more than 5% of patients who received Omegaven and with a higher incidence than the comparator group are: vomiting, agitation, bradycardia, apnea, viral infection, erythema, rash, abscess, neutropenia, hypertonia and incision site erythema. Patients had a complicated medical and surgical history prior to receiving Omegaven treatment and the mortality was 13%. Underlying clinical conditions prior to the initiation of Omegaven therapy included prematurity, low birth weight, necrotizing enterocolitis, short bowel syndrome, ventilator dependence, coagulopathy, intraventricular hemorrhage, and sepsis.

Twelve (6%) Omegaven-treated patients were listed for liver transplantation (1 patient was listed 18 days before treatment, and 11 patients after a median of 42 days [range: 2 days to 8 months] of treatment); 9 (5%) received a transplant after a median of 121 days (range: 25 days to 6 months) of treatment, and 3 (2%) were taken off the waiting list because cholestasis resolved.

One hundred thirteen (60%) Omegaven-treated patients reached DBil levels less than 2 mg/dL and AST or ALT levels less than 3 times the upper limit of normal, with median AST and ALT levels for Omegaven-treated patients at 89 and 65 U/L, respectively, by the end of the study.

Median hemoglobin levels and platelet counts for Omegaven-treated patients at baseline were 10.2 g/dL and 173 × 10^9/L, and by the end of the study these levels were 10.5 g/dL and 217 × 10^9/L, respectively. Adverse reactions associated with bleeding were experienced by 74 (39%) of Omegaven-treated patients.

Median glucose levels at baseline and the end of the study were 86 and 87 mg/dL for Omegaven-treated patients, respectively. Hyperglycemia was experienced by 13 (7%) Omegaven-treated patients.

Median triglyceride levels at baseline and the end of the study were 121 mg/dL and 72 mg/dL for Omegaven-treated patients respectively. Hypertriglyceridemia was experienced by 5 (3%) Omegaven-treated patients.

The triene:tetraene (Mead acid:arachidonic acid) ratio was used to monitor essential fatty acid status in Omegaven-treated patients only in Study 1 (n = 123). The median triene:tetraene ratio was 0.02 (interquartile range: 0.01 to 0.03) at both baseline and the end of the study. Blood samples for analysis may have been drawn while the lipid emulsion was being infused and patients received enteral or oral nutrition.

Postmarketing Experience

The following adverse reaction has been identified with use of Omegaven in another country. Life-threatening hemorrhage following a central venous catheter change was reported in a 9-month-old infant with intestinal failure who received PN with Omegaven as the sole lipid source; he had no prior history of bleeding, coagulopathy, or portal hypertension.

To report SUSPECTED ADVERSE REACTIONS, contact Fresenius Kabi USA, LLC, at 1-800-551-7176, option 5, or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

Prolonged bleeding time has been reported in patients taking antiplatelet agents or anticoagulants and oral omega-3 fatty acids. Periodically monitor bleeding time in patients receiving Omegaven and concomitant antiplatelet agents or anticoagulants.

USE IN SPECIFIC POPULATIONS

- Pregnancy: There are no available data on Omegaven use in pregnant women to establish a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. Animal reproduction studies have not been conducted with fish oil triglycerides. The estimated background risk of major birth defects and miscarriage in the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the US 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.
- Lactation: No data available regarding the presence of fish oil triglycerides from Omegaven in human milk, the effects on the breastfed infant, or the effects on milk production. Lactating women receiving oral omega-3 fatty acids have been shown to have higher levels of omega-3 fatty acids in their milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Omegaven, and any potential adverse effects of Omegaven on the breastfed infant.
- Pediatric Use: The safety of Omegaven was established in 189 pediatric patients (19 days to 15 years of age). The most common adverse reactions in Omegaven-treated patients were vomiting, agitation, bradycardia, apnea and viral infection. In the postmarketing setting, clinical decompensation with rapid infusion of lipid injectable emulsions in neonates and infants, sometimes fatal has been reported. Preterm neonates and infants who receive treatment with Omegaven may be at risk of aluminum toxicity and other metabolic abnormalities.
- Geriatric Use: Clinical trials of Omegaven did not include patients 65 years of age and older.

OVERDOSAGE

In the event of an overdose, serious adverse reactions may occur. Stop the infusion of Omegaven until triglyceride levels have normalized and any 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 serum.

SMOFLIPID (lipid injectable emulsion), for intravenous use

BRIEF SUMMARY OF PRESCRIBING INFORMATION

This brief summary does not include all the information needed to use SMOFlipid safely and effectively. Please see full prescribing information for intravenous use at www.FreseniusKabiNutrition.com/SMOFlipidPI.

INDICATIONS AND USAGE

SMOFlipid is indicated in adult and pediatric patients, including term and preterm neonates, as a source of calories and essential fatty acids for parenteral nutrition (PN) when oral or enteral nutrition is not possible, insufficient, or contraindicated.

DOSAGE AND ADMINISTRATION

The recommended daily dosage and initial and maximum infusion rates for pediatric and adult patients are provided in Table 1. Do not exceed the recommended maximum infusion rate in Table 1. The recommended duration of infusion for SMOFlipid will vary depending on the clinical situation. Adjust the administration flow rate by taking into account the dose being administered, the daily volume/intake, and the duration of the infusion.

SMOFlipid 1000 mL is supplied as a Pharmacy Bulk Package for admixing only and is not for direct infusion. Prior to administration, transfer to a separate PN container for individual patient use. Use a non-vented, non-DEHP 1.2 micron in-line filter during administration. Protect the admixed PN solution from light.

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*)	Initial 0.5 to 1 g/kg/day not to exceed 3 g/kg/day**	0.1 to 0.2 mL/kg/hour for the first 15 to 30 minutes; gradually increase to the required rate after 30 minutes	0.75 mL/kg/hour
Pediatric patients 2 to <12 years of age	Initial 1 to 2 g/kg/day not to exceed 3 g/kg/day**	0.2 to 0.4 mL/kg/hour for the first 15 to 30 minutes; gradually increase to the required rate after 30 minutes	0.75 mL/kg/hour
Pediatric patients 12 to 17 years of age	Initial 1 g/kg/day not to exceed 2.5 g/kg/day**	0.2 to 0.4 mL/kg/hour for the first 15 to 30 minutes; gradually increase to the required rate after 30 minutes	0.75 mL/kg/hour
Adults	1 to 2 g/kg/day not to exceed 2.5 g/kg/day**	0.2 mL/kg/hour for the first 15 to 30 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 newborn infants. The neonatal period for term and post-term infants is the day of birth plus 27 days. For preterm infants, 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 not exceed a maximum of 60% of total energy requirements

CONTRAINDICATIONS

- Known hypersensitivity to fish, egg, soybean, peanut or to any of the active or inactive ingredients in SMOFlipid.
- Severe disorders of lipid metabolism characterized by hypertriglyceridemia (serum triglycerides >1,000 mg/dL).

WARNINGS AND PRECAUTIONS

- 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.

  Strictly adhere to the recommended total daily dosage; the hourly infusion rate should not exceed 0.75 mL/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 of poor clearance of lipids from the circulation occur, stop the infusion and initiate a medical evaluation.

- Parenteral Nutrition-Associated Liver Disease and Other Hepatobiliary Disorders.

  Risk of Parenteral Nutrition-Associated Liver Disease (PNALD): PNALD, or Intestinal failure-associated liver disease (IFALD), can present as cholestasis or hepatic stenosis 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 SMOFlipid, 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 less frequently in SMOFlipid-treated patients than in 100% soybean oil lipid emulsion-treated patients.

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

  Other Hepatobiliary Disorders

  Hepatobiliary disorders including cholecystitis and cholelithiasis have developed in some parenteral nutrition-treated patients without preexisting liver disease. Monitor liver tests when administering SMOFlipid. Patients developing signs of hepatobiliary disorders should be assessed early to determine whether these conditions are related to SMOFlipid use.

- Hypersensitivity Reactions: SMOFlipid contains soybean oil, fish oil, and egg phospholipids, which may cause hypersensitivity reactions. Cross reactions have been observed between soybean and peanut. SMOFlipid is contraindicated in patients with known hypersensitivity to fish, egg, soybean, peanut, or any of the active or inactive ingredients in SMOFlipid. If a hypersensitivity reaction occurs, stop infusion of SMOFlipid immediately and initiate appropriate treatment and supportive measures.
- Infections: Lipid emulsions, such as SMOFlipid, can support microbial growth and are 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 SMOFlipid. 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.
- Fat Overload Syndrome: This is a rare condition that has been reported with intravenous lipid 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 SMOFlipid. The syndrome is usually reversible when the infusion of the lipid emulsion is stopped.

- 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.
- Hypertriglyceridemia: The use of SMOFlipid 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 SMOFlipid. In addition, patients with hypertriglyceridemia may have worsening of their hypertriglyceridemia with administration of SMOFlipid. 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 SMOFlipid 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.

- Aluminum Toxicity: SMOFlipid 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 infants are at greater risk because their kidneys are immature, and they require large amounts of calcium and phosphate solutions, which 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 can accumulate aluminum at levels associated with central nervous system and bone toxicity. Tissue loading may occur at even lower rates of administration.
- Essential Fatty Acid Deficiency: Treatment-emergent cases of moderate or severe essential fatty acid deficiency (EFAD) (defined as the triene [Mead acid] to tetraene [arachidonic acid] ratio >0.2 and >0.4, respectively) were not observed in pediatric clinical trials of SMOFlipid up to 28 days. However, cases of EFAD have been reported in adults and pediatric patients in the postmarketing period with the use of SMOFlipid. The median time to onset was greater than 28 days among cases that reported time to onset. Monitor patients for laboratory evidence (e.g., abnormal fatty acid levels) and clinical symptoms of EFAD (e.g., skin manifestations and poor growth) because these signs may emerge before laboratory evidence of EFAD is confirmed. Laboratory testing using the triene to tetraene ratio may not be adequate to diagnose EFAD, and assessment of individual fatty acid levels may be needed. Ensure patients are receiving recommended dosages of SMOFlipid to prevent EFAD.
- Monitoring/Laboratory Tests: Throughout treatment monitor serum triglycerides, fluid and electrolyte status, blood glucose, liver and kidney function, coagulation parameters, and complete blood count including platelets.

  The lipids contained in SMOFlipid may interfere with some laboratory blood tests (e.g., hemoglobin, lactate dehydrogenase [LDH], bilirubin, and oxygen saturation) if blood is sampled before lipids have cleared from the bloodstream. Conduct these blood tests at least 6 hours after stopping the infusion. SMOFlipid contains vitamin K that may counteract anticoagulant activity.

ADVERSE REACTIONS

Most common adverse drug reactions >1% of adult patients who received SMOFlipid from clinical trials were nausea, vomiting, hyperglycemia, flatulence, pyrexia, abdominal pain, increased blood triglycerides, hypertension, sepsis, dyspepsia, urinary tract infection, anemia, and device-related infection.

Less common adverse reactions in ≤1% of adult patients who received SMOFlipid were dyspnea, leukocytosis, diarrhea, pneumonia, cholestasis, dysgeusia, increased blood alkaline phosphatase, increased gamma-glutamyltransferase, increased C-reactive protein, tachycardia, liver function test abnormalities, headache, pruritis, dizziness, rash, and thrombophlebitis.

The most common adverse drug reactions in >1% of pediatric patients who received SMOFlipid were anemia, vomiting, gamma-glutamyltransferase increased, nosocomial infection, cholestasis, pyrexia, C-reactive protein increased, hyperbilirubinemia, abdominal pain, bilirubin conjugated increased, diarrhea, tachycardia, thrombocytopenia, hyperglycemia, and sepsis.

Less common adverse reactions in ≤1% of pediatric patients who received SMOFlipid were decreased hematocrit, metabolic acidosis, increased blood triglycerides, infection, increased blood alkaline phosphatase, increased alanine aminotransferase, fluid overload, hypertension, hypertriglyceridemia, and rash.

The following adverse reactions have been identified during post-approval use of SMOFlipid in countries where it is registered. Cardiac disorders: palpitations; General disorders and administration site conditions: chills, chest pain, malaise; Hepatobiliary disorders: cholestasis; Infections and infestations: infection; Metabolism and nutrition disorders: fatty acid deficiency; Respiratory, thoracic and mediastinal disorders: dyspnea; Skin and subcutaneous tissue disorders: hyperhidrosis; Vascular disorders: phlebitis.

To report SUSPECTED ADVERSE REACTIONS, contact Fresenius Kabi USA, LLC at 1-800-551-7176, option 5, or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

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

USE IN SPECIFIC POPULATIONS

- Pregnancy and Lactation: Administration of the recommended dose of SMOFlipid is not expected to cause major birth defects, miscarriage, or other adverse maternal or fetal outcomes. No animal reproduction studies have been conducted with SMOFlipid. Administration of the recommended dose of SMOFlipid is not expected to cause harm to a breastfed infant. There are no data on the presence of SMOFlipid in human or animal milk or its effects on milk production.
- Pediatric Use: The safety and effectiveness of SMOFlipid have been established as a source of calories and essential fatty acids for parenteral nutrition when oral or enteral nutrition is not possible, insufficient, or contraindicated in pediatric patients, including term and preterm neonates. Use of SMOFlipid in neonates is supported by evidence from short-term (i.e., 1- to 4-week) studies, and one study following neonates beyond 4 weeks. Use of SMOFlipid in older pediatric patients is supported by evidence from a short-term (i.e., <28 days) study in pediatric patients 28 days to 12 years of age and additional evidence from studies in adults. The most common adverse reactions in SMOFlipid-treated pediatric patients were anemia, vomiting, gamma-glutamyltransferase increased, and nosocomial infection. PNALD, also referred to as IFALD, has been reported in pediatric patients who received SMOFlipid for more than 2 weeks. PNAC (a precursor to PNALD) was reported less frequently in SMOFlipid-treated patients compared to soybean oil lipid emulsion-treated patients in Pediatric Study 1. Although clinically significant cases of EFAD were not observed during short-term use in pediatric clinical studies, cases of EFAD have been reported with the use of SMOFlipid in the postmarketing setting. Monitor pediatric patients for laboratory evidence of EFAD because they may be particularly vulnerable to neurologic complications if adequate amounts of essential fatty acids are not provided. In the post marketing setting, clinical decompensation with rapid infusion of intravenous lipid emulsion in neonates and infants, sometimes fatal has been reported. Because of immature renal function, preterm infants receiving prolonged treatment with SMOFlipid may be at risk for aluminum toxicity.
- Geriatric Use: Energy expenditure and requirements may be lower for older adults than younger patients. Of the 354 adult patients in clinical studies of SMOFlipid, 35% were >65 years of age and 10% were >75 years of age. No overall differences in the safety and efficacy of SMOFlipid were observed between these patients and younger patients, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity in some older patients cannot be ruled out.

OVERDOSAGE

In the event of an overdose, serious adverse reactions may result. Stop the SMOFlipid infusion 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.

KABIVEN® (Amino Acids, Electrolytes, Dextrose, and Lipid Injectable Emulsion), for intravenous use

PERIKABIVEN® (Amino Acids, Electrolytes, Dextrose, and Lipid Injectable Emulsion), for intravenous use

BRIEF SUMMARY OF PRESCRIBING INFORMATION

This brief summary does not include all the information needed to use KABIVEN and PERIKABIVEN safely and effectively. Please see full prescribing information for KABIVEN® (Amino Acids, Electrolytes, Dextrose, and Lipid Injectable Emulsion), for intravenous use and PERIKABIVEN® (Amino Acids, Electrolytes, Dextrose, and Lipid Injectable Emulsion), for intravenous use at label www.FreseniusKabiNutrition.com/KabivenPI and www.FreseniusKabiNutrition.com/PerikabivenPI.

INDICATIONS AND USAGE

KABIVEN and PERIKABIVEN are each 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 and PERIKABIVEN may be used to prevent essential fatty acid deficiency or treat negative nitrogen balance in adult patients.

Limitations of Use

Neither KABIVEN nor PERIKABIVEN are 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.

DOSAGE AND ADMINISTRATION

KABIVEN is indicated for intravenous infusion into a **central vein**. PERIKABIVEN is indicated for intravenous infusion into a **peripheral or central vein**. It is recommended to mix the contents thoroughly by inverting the bags upside down to ensure a homogenous admixture. Ensure the vertical seals between chambers are broken and the contents of all three chambers for KABIVEN and PERIKABIVEN are mixed together prior to infusion. The dosage of KABIVEN and PERIKABIVEN 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. Prior to administration of KABIVEN and PERIKABIVEN, correct severe fluid, electrolyte and acid-base disorders. Before starting the infusion, obtain serum triglyceride levels to establish the baseline value. The recommended dosage of KABIVEN in adults is 19 to 38 mL/kg/day. The recommended dosage of PERIKABIVEN in adults is 27 to 40 mL/kg/day. The maximum daily dosage of KABIVEN and PERIKABIVEN in adults should not exceed 40 mL/kg/day. Do not exceed the recommended maximum infusion rate of 2.6 mL/kg/hour for KABIVEN and 3.7 mL/kg/hour for PERIKABIVEN.

CONTRAINDICATIONS

KABIVEN and PERIKABIVEN are 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.
- Patients with known hypersensitivity to egg, soybean, peanut or any of the active or inactive ingredients.
- Patients with severe disorders of lipid metabolism characterized by hypertriglyceridemia (serum triglyceride concentration >1,000 g/dL).
- 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.

WARNINGS AND PRECAUTIONS (also see BOXED WARNING)

- Clinical Decompensation with Rapid Infusion of Lipid Injectable 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 lipid injectable emulsions. Hypertriglyceridemia was commonly reported. Preterm and small for gestational age infants have poor clearance of lipid injectable emulsions and increased free fatty acid plasma levels following infusion.
- 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 and PERIKABIVEN) 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.

  Monitor liver tests in patients treated with KABIVEN and PERIKABIVEN 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 and PERIKABIVEN. Patients developing signs of hepatobiliary disorders should be assessed early to determine whether these conditions are related to KABIVEN or PERIKABIVEN use.
- 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 PN.

  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 the catheter for precipitates, prior to administration as well as periodically during the administration. If signs of respiratory distress or pulmonary embolism occur, stop the infusion and initiate a medical evaluation.
- Hypersensitivity Reactions: KABIVEN and PERIKABIVEN contain soybean oil, which may cause hypersensitivity reactions. Cross reactions have been observed between soybean and peanut. KABIVEN and PERIKABIVEN are contraindicated in patients with known hypersensitivity to egg, soybean, peanut, or any of the active or inactive ingredients. If a hypersensitivity reaction occurs, stop the infusion immediately and initiate appropriate treatment and supportive measures.
- Precipitation with Ceftriaxone: Precipitation of ceftriaxone-calcium can occur when ceftriaxone is mixed with calcium-containing PN solutions, such as KABIVEN or PERIKABIVEN in the same intravenous administration line. **Do not** administer ceftriaxone simultaneously with KABIVEN or PERIKABIVEN via Y-site. However, in patients other than neonates, ceftriaxone and KABIVEN or PERIKABIVEN may be administered sequentially if the infusion lines are thoroughly flushed between infusions with a compatible fluid.

  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.
- Infections: PN, such as KABIVEN and PERIKABIVEN, 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 and PERIKABIVEN. 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.
- Fat Overload Syndrome: Fat overload syndrome is a rare condition that has been reported with 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 dosage 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 or PERIKABIVEN. The syndrome is usually reversible when the infusion including the lipid emulsion is stopped.
- 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.

- Diabetes/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 or PERIKABIVEN. Insulin may be administered or adjusted to maintain optimal blood glucose levels during KABIVEN or PERKABIVEN administration.
- Hypertriglyceridemia: The use of KABIVEN and PERIKABIVEN are 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 or PERIKABIVEN. In addition, patients with hypertriglyceridemia may have worsening of their hypertriglyceridemia with administration of KABIVEN and PERIKABIVEN. Excessive dextrose administration may further increase such risk. Evaluate the patient's 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 or PERIKABIVEN 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.
- 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. Remove the catheter as soon as possible if thrombophlebitis develops.

  PERIKABIVEN is indicated for **peripheral administration or may be infused into a central vein, however**, peripheral catheters should not be used for solutions with osmolarity of ≥ 900 mOsm/L. The catheter should be removed as soon as possible if thrombophlebitis develops.
- 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 and PERIKABIVEN. In patients with decreased renal function with electrolyte imbalance or fluid overload, the KABIVEN or PERIKABIVEN should be used with caution, and the 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 or PERIKABIVEN dosage or other treatment options.
- Aluminum Toxicity: KABIVEN and PERIKABIVEN contain no more than 25 mcg/L of aluminum. The aluminum contained in KABIVEN and PERIKABIVEN 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 PN products.
- Monitoring/Laboratory Tests: Monitor fluid status closely in patients with pulmonary edema or heart failure. Throughout treatment monitor serum triglycerides, fluid and electrolyte status, serum osmolarity, blood glucose, liver and kidney function, blood count (including platelets) and coagulation parameters. KABIVEN and PERIKABIVEN contain Vitamin K that may counteract anticoagulant activity.

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

ADVERSE REACTIONS

Clinical Trials Experience

Adverse reactions occurring in >1% of patients who received **KABIVEN** were nausea, pyrexia, hypertension, vomiting, decreased hemoglobin, decreased total protein, hypokalemia, decreased blood potassium, increased gamma-glutamyltransferase, hyperglycemia, increased blood alkaline phosphatase, decreased blood calcium, prolonged prothrombin time, pruritus and tachycardia.

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.

Adverse reactions occurring in >2% of patients who received **PERIKABIVEN** were hyperglycemia, hypokalemia, pyrexia, increased blood triglycerides, phlebitis, nausea, pruritus, increased gamma-glutamyltransferase, increased blood alkaline phosphatase, increased alanine aminotransferase, increased blood glucose, increased C-reactive protein, increased blood urea and hypoalbuminemia.

Less common adverse reactions in ≤1% of patients who received **PERIKABIVEN** were hyperkalemia, hypomagnesaemia, hypernatremia, tachycardia, hypertension, thrombophlebitis, vomiting, jaundice, rash and increased blood bilirubin.

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 and PERIKABIVEN. 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.

Post-Marketing Experience

The following additional adverse reactions have been identified during post-approval use of **KABIVEN** in countries where it is registered. Hepatobiliary disorders: cholestasis. Infections and infestations: infection. Nervous system disorders: subependymal hemorrhage.

The following additional adverse reactions have been identified during post-approval use of **PERIKABIVEN** in countries where it is registered. Gastrointestinal disorders: abdominal distension, abdominal pain. General disorders and administration site conditions: chest tightness. Hepatobiliary disorders: cholestasis. Immune system disorders: allergic reaction, anaphylaxis. Infections and infestations: infection. Vascular disorders: flushed face.

To report SUSPECTED ADVERSE REACTIONS, contact Fresenius Kabi USA, LLC at 1-800-551-7176, option 5, or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

Ceftriaxone: Precipitation of ceftriaxone-calcium can occur when ceftriaxone is mixed with calcium-containing PN solutions, such as KABIVEN and PERIKABIVEN, in the same intravenous administration line. Do not administer ceftriaxone simultaneously with KABIVEN or PERIKABIVEN via a Y-site. However, ceftriaxone and KABIVEN or PERIKABIVEN may be administered sequentially if the infusion lines are thoroughly flushed between infusions with a compatible fluid. 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.

Coumarin and Coumarin Derivatives: The soybean oil present in KABIVEN and PERIKABIVEN 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 or PERIKABIVEN and coumarin or coumarin derivatives.

USE IN SPECIFIC POPULATIONS

- Pregnancy: The limited available data on the use of KABIVEN and PERIKABIVEN in pregnant women are not sufficient to inform a drug-associated risk. There are clinical considerations if KABIVEN or PERIKABIVEN is used in pregnant women. Animal reproduction studies have not been conducted with KABIVEN and PERIKABIVEN.
- Lactation: There are no data available to assess the presence of KABIVEN and PERIKABIVEN 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 or PERIKABIVEN, and any potential adverse effects of KABIVEN and PERIKABIVEN on the breastfed child or from the underlying maternal condition.
- Pediatric Use: The safety and effectiveness of KABIVEN and PERIKABIVEN has not been established in pediatric patients of any age. In the postmarketing setting, clinical decompensation with rapid infusion of lipid injectable emulsions in neonates and infants, sometimes fatal has been reported.
- Geriatric Use: Clinical studies of KABIVEN and PERIKABIVEN 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.

OVERDOSAGE

In the event of an overdose, serious adverse reactions may result. Stop the infusion of KABIVEN or PERIKABIVEN 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.

Intralipid®
(lipid injectable emulsion, USP 20%)

Please scan this QR code or visit https://qrco.de/be3wh4 to see the full Prescribing Information

INTRALIPID® 20% (a 20% Intravenous Fat Emulsion) and INTRALIPID 20% and 30% Pharmacy Bulk Packages (a 20% and 30% Intravenous Fat Emulsion)

BRIEF SUMMARY OF PRESCRIBING INFORMATION

This brief summary does not include all the information needed to use Intralipid safely and effectively. Please see full prescribing information for intravenous use at www.freseniuskabinutrition.com/IntralipidPI.

INDICATIONS AND USAGE
Intralipid® 20% (A 20% Intravenous Fat Emulsion) 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).

Intralipid 20% Pharmacy Bulk Package (A 20% Intravenous Fat Emulsion) and Intralipid 30% Pharmacy Bulk Package (A 30% Intravenous Fat Emulsion) are indicated for use in a pharmacy admixture program for the preparation of three-in-one or total nutrient admixtures (TNAs) to provide a source of calories and essential fatty acids for adult and pediatric patients requiring parenteral nutrition and as a source of essential fatty acids for prevention of essential fatty acid deficiency (EFAD).

INTRALIPID 20% and 30% PHARMACY BULK PACKAGE ARE NOT INTENDED FOR DIRECT INTRAVENOUS ADMINISTRATION.

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

DOSAGE AND ADMINISTRATION
The recommended nutritional requirements of lipid and recommended dosages of Intralipid 20% 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. Do not exceed the recommended maximum infusion rate in Table 1. Use a 1.2 micron in-line filter during administration. Protect the admixed PN solution from light.

Table 1: Recommended Pediatric and Adult Dosage and Infusion Rate for Intralipid 20%

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*)	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.

Dosage for Intralipid 30%
Adult Patients: The initial infusion rate of the nutrient admixture in adults should be the equivalent of 0.1 g fat/minute (0.1 mL/kg/hour) for the first 15 to 30 minutes of infusion. If no untoward reactions occur (see ADVERSE REACTIONS section), the infusion rate of the nutrient admixture can be increased to be equivalent to 0.2 g fat/minute (0.2 mL/kg/hour). For adults, the admixture should not contain more than 330 mL of Intralipid 30% on the first day of therapy. If the patient has no untoward reactions, the dose can be increased on the following day. The daily dosage should not exceed 2.5 g of fat/kg of body weight (8.3 mL of Intralipid 30% per kg). Intralipid 30% 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/hour (0.3 mL/kg/hour).

Pediatric Patients: The dosage for premature infants starts at 0.5 g fat/kg body weight/24 hours (1.7 mL) Intralipid 30% and may be increased in relation to the infant's ability to eliminate fat. The maximum recommended dosage is 3 g fat/kg/24 hours. The initial rate of infusion of the nutrient admixture in older pediatric patients should be no more than 0.01 g fat/minute for the first 10 to 15 minutes. If no untoward reactions occur, the rate can be changed to permit infusion of 0.1 g of fat/kg/hour. The daily dosage should not exceed 3 g of fat/kg of body weight. Intralipid (equivalent to 0.125 g/kg/hour) should make up no more than 60% of the total caloric input to the patient.

CONTRAINDICATIONS
Intralipid is contraindicated in patients with:
- Known hypersensitivity to egg, soybean, peanut, or any of the active or inactive ingredients in Intralipid
- Severe disorders of lipid metabolism characterized by hypertriglyceridemia (serum triglyceride > 1,000 mg/dL)
- Disturbances of normal fat metabolism such as pathologic hyperlipemia, lipoid nephrosis or acute pancreatitis if accompanied by hyperlipidemia

WARNINGS AND PRECAUTIONS
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 for Intralipid 20% should not exceed 0.75 mL/kg/hour, and for Intralipid 30%, the hourly infusion rate should not exceed 0.5 mL/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.

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.

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 contains soybean oil and egg phospholipids, which may cause hypersensitivity reactions. Cross reactions have been observed between soybean and peanut. Intralipid is contraindicated in patients with known hypersensitivity to egg, soybean, peanut or any of the active or inactive ingredients in Intralipid. If a hypersensitivity reaction occurs, stop infusion of Intralipid immediately and initiate appropriate treatment and supportive measures.

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.

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.

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.

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.

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.

Monitoring/Laboratory Tests
Monitor fluid status closely in patients with pulmonary edema or heart failure. Throughout treatment, monitor serum triglycerides, 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.

ADVERSE REACTIONS
The most common adverse reactions in >1% of adult patients treated with Intralipid/soybean oil emulsion include nausea, vomiting, pyrexia, hypertension, headache, hyperglycemia, abdominal pain, flatulence, increased blood triglycerides, sepsis, diarrhea, pneumonia, pruritus and increased gamma-glutamyltransferase.

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 most common adverse reactions in >1% of pediatric patients treated with Intralipid include anemia, vomiting, increased gamma-glutamyltransferase, cholestasis, pyrexia, increased C-reactive protein, hyperbilirubinemia, increased conjugated bilirubin, nosocomial infection, increased blood alkaline phosphatase, abdominal pain, decreased hematocrit, metabolic acidosis, diarrhea, tachycardia, thrombocytopenia, increased alanine aminotransferase, increased aspartate aminotransferase and PNALD.

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.

The following adverse reactions from voluntary reports have been reported with Intralipid: 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; Vascular disorders: phlebitis; Blood and lymphatic system disorders: hypercoagulability.

To report SUSPECTED ADVERSE REACTIONS, contact Fresenius Kabi USA, LLC at 1-800-551-7176, option 5, or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

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.

USE IN SPECIFIC POPULATIONS
- Pregnancy and lactation: 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. Administration of the recommended dose of Intralipid is not expected to cause harm to a breastfed infant.
- Pediatric use: 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. 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. 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. In the postmarketing setting, clinical decompensation with rapid infusion of intravenous lipid emulsion in neonates and infants, sometimes fatal, has been reported. Because of immature renal function, preterm neonates receiving prolonged treatment with Intralipid may be at risk for aluminum toxicity.
- 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.

OVERDOSAGE
In the event of an overdose, serious adverse reactions may result. 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.

Fresenius Kabi Nutrition will continue to pioneer PN products and bring innovative alternative lipid emulsions to market

The **FIRST** and **ONLY** fish oil ILE for pediatrics

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Three Corporate Drive,
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Phone: 1.888.386.1300
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