FRESENIUS KABI
caring for life

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

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

Kabiven® and Perikabiven®

Composition Chart*

Kabiven (central PN)					Perikabiven (peripheral or central PN)	
Volume (mL)	1026	1540	2053	2566	1440	1920
Amino Acids (g)	34	51	68	85	34	45
Nitrogen (g)	5.4	8.2	10.9	13.6	5.4	7.2
Dextrose (g)	110	165	220	275	107	143
Lipids (g)	40	60	80	100	51	68
Total kcal	910	1365	1820	2275	1010	1346
Electrolytes†						
Sodium (mEq)	32	48	64	80	32	42
Potassium (mEq)	24	35	47	59	24	33
Magnesium (mEq)	8	12	16	20	8	11
Acetate (mEq)	39	59	78	98	39	52
Chloride (mEq)	46	69	92	115	46	61
Sulfate (mEq)	8	12	16	20	8	11
Calcium (mEq)	4	6	8	10	4	5
Phosphorus (mmol)	10	15	20	25	11	14
Osmolarity (mOsm/L)	1060	1060	1060	1060	750	750

*Calculations in this table are per bag and differ from Table 2 in the Kabiven/Perikabiven Prescribing Information that are calculated per 1000 mL or 100 mL.
†Provided as: sodium acetate, potassium chloride, sodium glycero-phosphate, magnesium sulfate, and calcium chloride.

WARNING: DEATH IN PRETERM INFANTS

- **Deaths in preterm infants after infusion of intravenous lipid emulsions have been reported in the medical literature.**
- **Autopsy findings included intravascular fat accumulation in the lungs.**
- **Preterm infants and low-birth-weight infants have poor clearance of intravenous lipid emulsion and increased free fatty acid plasma levels following lipid emulsion infusion.**

Please see Brief Summary of Prescribing Information, including **Boxed Warning**, for Kabiven and Perikabiven on the next page.

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, including Boxed Warning 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 (fda.gov).

WARNING: DEATH IN PRETERM INFANTS

- **Deaths in preterm infants after infusion of intravenous lipid emulsions have been reported in the medical literature.**
- **Autopsy findings included intravascular fat accumulation in the lungs.**
- **Preterm infants and low-birth-weight infants have poor clearance of intravenous lipid emulsion and increased free fatty acid plasma levels following lipid emulsion infusion.**

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.

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 proteins, peanut proteins, or to any of the active ingredients or excipients.
- Patients with severe hyperlipidemia or severe disorders of lipid metabolism characterized by hypertriglyceridemia (serum triglyceride concentration >1,000 g/dL).
- 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)

- Death in Preterm Infants: Deaths in preterm infants after infusion of intravenous lipid emulsions containing only soybean oil have been reported in the medical literature. Autopsy findings included intravascular lipid accumulation in the lungs. 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. The safe and effective use of KABIVEN and PERIKABIVEN injection in pediatric patients, including preterm infants, has not been established. KABIVEN and PERIKABIVEN are not recommended for use in pediatric patients under the age of 2 years including preterm infants.
- 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 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 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 protein, or to 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 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 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.
- Laboratory Tests: Monitor serum triglycerides, essential fatty acids, fluid and electrolyte status, serum osmolarity, blood glucose, liver tests, kidney function, coagulation parameters, and complete blood count periodically during treatment. Supplementation of essential fatty acids may be needed.
- 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**. 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 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.
- 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.
- 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 total parenteral nutrition products.
- Interference with Laboratory Tests: The lipids contained in KABIVEN and PERIKABIVEN may interfere with some laboratory blood tests (e.g., hemoglobin, triglycerides, bilirubin, LDH, and oxygen saturation), if blood is sampled before lipids in KABIVEN or PERIKABIVEN have been cleared from the bloodstream. Lipids are normally cleared after a period of 5 to 6 hours once the infusion is stopped. Therefore, conduct these blood tests at least 6 hours after the infusion is stopped.

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 parenteral nutrition 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 K1 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. Deaths in preterm infants after infusion of intravenous lipid emulsion have been reported. Patients, particularly preterm infants, are at risk for aluminum toxicity.
- 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.
- Hepatic Impairment: In patients with impaired liver function KABIVEN and PERIKABIVEN should be administered with caution. Frequent clinical evaluation and laboratory tests to monitor liver function such as bilirubin and liver function parameters should be conducted.
- Renal Impairment: In patients with impaired renal function, KABIVEN and PERIKABIVEN should be administered with caution. Frequent clinical evaluation and laboratory tests to monitor renal function such as serum electrolytes (especially phosphate and potassium) and fluid balance should be conducted.

OVERDOSAGE

In the event of an overdose, fat overload syndrome 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.

To order: **1-888-386-1300**
Med Info phone: **1-800-551-7176** (option 4)

www.FreseniusKabiNutrition.com/products/kabiven-perikabiven

Med Info email: **Nutrition.MedInfo.USA@fresenius-kabi.com**
Information on coding and billing: **1-833-KABICARE (1-833-522-4227)**

www.kabicare.us

FRESENIUS KABI
caring for life

Fresenius Kabi USA, LLC
Three Corporate Drive,
Lake Zurich, IL 60047
Phone: 1.888.386.1300
www.fresenius-kabi.com/us

Fresenius Kabi USA Nutrition