

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)	100	150	200	250	97	130
Lipids (g)	40	60	80	100	51	68
Total kcal	870	1310	1745	2180	970	1300
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 1000ml or 100ml.

** 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.

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® (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 www.FreseniusKabiNutrition.com.

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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 is 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 is contraindicated in patients with known hypersensitivity to egg, soybean proteins, peanut proteins, corn or corn products or to any of the active substances or excipients. Severe hyperlipidemia or severe disorders of lipid metabolism characterized by hypertriglyceridemia (serum triglyceride concentration $\geq 1,000$ mg/dL). Inborn error of amino acid metabolism. Cardiopulmonary instability (including pulmonary edema, cardiac insufficiency, myocardial infarction, acidosis and hemodynamic instability requiring significant vasopressor support). Hemophagocytic syndrome.

WARNINGS AND PRECAUTIONS (also see BOXED WARNING)

- **Death in Preterm Infants:** Deaths in preterm infants after infusion of intravenous lipid emulsions have been reported. 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 is not recommended for use in pediatric patients under the age of 2 years including preterm infants.
- **Hypersensitivity Reactions:** Stop infusion immediately and treat patient accordingly if signs or symptoms of a hypersensitivity or allergic reaction develop. Signs or symptoms may include: tachypnea, dyspnea, hypoxia, bronchospasm, tachycardia, hypotension, cyanosis, vomiting, nausea, headache, sweating, dizziness, altered mentation, flushing, rash, urticaria, erythema, pyrexia and chills.
- **Infections:** Patients who require parenteral nutrition are at high risk of infections due to malnutrition and their underlying disease state. Infection and sepsis may occur as a result of the use of intravenous catheters to administer parenteral nutrition, poor maintenance of catheters, or immunosuppressive effects of illness, drugs, and parenteral formulations. Decrease the risk of septic complications. Monitor for signs and symptoms (including fever and chills) of early infections, including laboratory test results (including leukocytosis and hyperglycemia) and frequent checks of the parenteral access device.
- **Fat Overload Syndrome:** Fat overload syndrome is a rare condition that has been reported with intravenous lipid emulsions. A reduced or limited ability to metabolize lipids accompanied by prolonged plasma clearance may result in a syndrome characterized by a sudden deterioration in the patient's condition accompanied by fever, anemia, leukopenia, thrombocytopenia, coagulation disorders, hyperlipidemia, liver fatty infiltration (hepatomegaly), deteriorating liver function, and central nervous system manifestations (e.g., coma).
- **Refeeding Syndrome:** Refeeding severely undernourished patients with parenteral nutrition may result in the refeeding syndrome, characterized by the intracellular shift of potassium, phosphorus, and magnesium as the patient becomes anabolic. Thiamine deficiency and fluid retention may also develop.

- **Diabetes/Hyperglycemia:** KABIVEN and PERIKABIVEN should be used with caution in patients with diabetes mellitus or hyperglycemia. With the administration of KABIVEN and PERIKABIVEN, hyperglycemia and hyperosmolar syndrome may result. Administration of dextrose at a rate exceeding the patient's utilization rate may lead to hyperglycemia, coma and death. Monitor blood glucose levels and treat hyperglycemia to maintain optimum levels while infusing KABIVEN or PERIKABIVEN.
- **Monitoring/Laboratory Tests:** Routine Monitoring: Monitor fluid status closely in patients with heart failure or pulmonary edema. Monitor serum triglycerides, fluid and electrolyte status, serum osmolarity, blood glucose, liver and kidney function, and blood count, including platelet and coagulation parameters, throughout treatment. In situations of severely elevated electrolyte levels stop KABIVEN or PERIKABIVEN until levels have been corrected. Essential Fatty Acids: Monitoring patients for signs and symptoms 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. Increasing essential fatty acid intake (enterally or parenterally) is effective in treating and preventing EFAD.
- **Vein Damage and Thrombosis:** KABIVEN is indicated for administration into a central vein only, such as the superior vena cava. The infusion of hypertonic nutrient injections into a peripheral vein may result in vein irritation, vein damage, and/or thrombosis.
- **Thrombophlebitis:** 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 primary complication of peripheral access is venous thrombophlebitis, which manifests as pain, erythema, tenderness or a palpable cord. The catheter should be removed as soon as thrombophlebitis develops.
- **Precipitation with Ceftriaxone:** Precipitation of ceftriaxone-calcium can occur when ceftriaxone is mixed with calcium-containing parenteral nutrition solutions, such as KABIVEN or PERIKABIVEN in the same intravenous administration line. Ceftriaxone must not be administered simultaneously with KABIVEN or PERIKABIVEN via a Y-site. However, ceftriaxone and KABIVEN or ceftriaxone and PERIKABIVEN may be administered sequentially if the infusion lines are thoroughly flushed between infusions with a compatible fluid.
- **Hepatobiliary Disorders:** Hepatobiliary disorders are known to develop in some patients without preexisting liver disease who receive parenteral nutrition, including cholecystitis, cholelithiasis, cholestasis, hepatic steatosis, fibrosis and cirrhosis, possibly leading to hepatic failure. The etiology of these disorders is thought to be multifactorial and may differ between patients. Increase of blood ammonia levels and hyperammonemia may occur in patients receiving amino acid solutions. In some patients this may indicate hepatic insufficiency or the presence of an inborn error of amino acid metabolism or hepatic insufficiency. Monitor liver function parameters and ammonia.
- **Electrolyte Imbalance and Fluid Overload in Renal Impairment:** Patients with renal impairment, such as pre-renal azotemia, renal obstruction and protein-losing nephropathy may be at increased risk of electrolyte and fluid volume imbalance. KABIVEN and PERIKABIVEN should be used with caution in patients with renal impairment. KABIVEN and PERIKABIVEN dosage may require adjustment with specific attention to fluid, protein and electrolyte content in these patients. Monitor renal function parameters.
- **Hypertriglyceridemia:** To evaluate the patient's capacity to eliminate and metabolize the infused lipid emulsion, measure serum triglycerides before the start of infusion (baseline value), with each increase in dosage, and regularly throughout treatment. Reduce dose of KABIVEN or PERIKABIVEN and monitor serum triglyceride levels in patients with serum triglyceride concentrations above 400 mg/dL to avoid the clinical consequences associated with hypertriglyceridemia. Serum triglyceride levels above 1,000 mg/dL have been associated with an increased risk of pancreatitis. Impaired lipid metabolism with hypertriglyceridemia may occur in conditions such as inherited lipid disorders, obesity, diabetes mellitus, and metabolic syndrome.
- **Aluminum Toxicity:** KABIVEN and PERIKABIVEN contains 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:** High levels of lipids in plasma may interfere with some laboratory blood tests such as hemoglobin, triglycerides, bilirubin, LDH, and oxygen saturation, if blood is sampled before lipid has been cleared from the bloodstream. Lipids are normally cleared after a lipid-free interval of 5 to 6 hours in most patients. KABIVEN and PERIKABIVEN contains Vitamin K1 which may interfere with anticoagulant activity.
- **Risk of Parenteral Nutrition Associated Liver Disease:** Parenteral Nutrition Associated Liver Disease (PNALD) has been reported in patients who receive parenteral nutrition for extended periods of time, especially preterm infants, and can present as cholestasis or steatohepatitis. The exact etiology is unknown and is likely multifactorial. Intravenously administered phytosterols (plant sterols) contained in plant-derived lipid formulations have been associated with development of PNALD although a causal relationship has not been established. If KABIVEN and PERIKABIVEN treated patients develop liver test abnormalities, consider discontinuation or dose reduction.

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 $\leq 1\%$ 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 $\leq 1\%$ of patients who received PERIKABIVEN were hyperkalemia, hypomagnesaemia, hypernatremia, tachycardia, hypertension, thrombophlebitis, vomiting, jaundice, rash and increased blood bilirubin.

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

Coumarin and Coumarin Derivatives, Including Warfarin: Anticoagulant activity may be counteracted; monitor laboratory parameters.

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 in pediatric patients has not been established. 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 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



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