Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Kabiven Peripheral emulsion for infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Kabiven Peripheral is available in a three chamber bag system. Each bag contains the following different volumes depending on the pack size.

	2400 ml	**1920 ml**	**1440 ml**
Glucose (Glucose 11%)	1475 ml	1180 ml	885 ml
Amino acids and electrolytes (Vamin 18 Novum)	500 ml	400 ml	300 ml
Fat emulsion (Intralipid 20%)	425 ml	340 ml	255 ml

This corresponds to the following total compositions:

Active ingredients	**2400 ml**	**1920 ml**	**1440 ml**
Purified soybean oil	85.0 g	68.0 g	51.0 g
Glucose monohydrate	178.0 g	143.0 g	107.0 g
Corresponding to Glucose (anhydrous)	162.0 g	130.0 g	97.0 g
Alanine	8.0 g	6.4 g	4.8 g
Arginine	5.6 g	4.5 g	3.4 g
Aspartic acid	1.7 g	1.4 g	1.0 g
Glutamic acid	2.8 g	2.2 g	1.7 g
Glycine	4.0 g	3.2 g	2.4 g
Histidine	3.4 g	2.7 g	2.0 g
Isoleucine	2.8 g	2.2 g	1.7 g
Leucine	4.0 g	3.2 g	2.4 g
Lysine hydrochloride	5.6 g	4.5 g	3.4 g
Corresponding to Lysine	4.5 g	3.6 g	2.7 g
Methionine	2.8 g	2.2 g	1.7 g
Phenylalanine	4.0 g	3.2 g	2.4 g
Proline	3.4 g	2.7 g	2.0 g
Serine	2.2 g	1.8 g	1.4 g
Threonine	2.8 g	2.2 g	1.7 g
Tryptophan	0.95 g	0.76 g	0.57 g
Tyrosine	0.12 g	0.092 g	0.069 g
Valine	3.6 g	2.9 g	2.2 g

Active ingredients	**2400ml**	**1920ml**	**1440ml**
Calcium chloride 2 H_2O	0.49 g	0.39 g	0.29 g
Corresponding to Calcium chloride	0.37 g	0.30 g	0.22 g
Sodium glycerophosphate (anhydrous)	2.5 g	2.0 g	1.5 g
Magnesium sulphate $7H_2O$	1.6 g	1.3 g	0.99 g
Corresponding to Magnesium sulphate	0.80 g	0.64 g	0.48 g
Potassium chloride	3.0 g	2.4 g	1.8 g
Sodium acetate 3 H_20	4.1 g	3.3 g	2.5 g
Corresponding to Sodium acetate	2.4 g	2.0 g	1.5 g

Corresponding to:

	2400 ml	**1920 ml**	**1440 ml**
o Amino acids	57.0 g	45.0 g	34.0 g
o Nitrogen	9.0 g	7.2 g	5.4 g
o Fat	85.0 g	68.0 g	51.0 g
o Carbohydrates			
- Glucose (anhydrous)	162.0 g	130.0 g	97.0 g
o Energy content			
- total	approx. 1700 kcal	1400 kcal	1000 kcal
- non protein	approx. 1500 kcal	1200 kcal	900 kcal
o Electrolytes			
- sodium	53.0 mmol	43.0 mmol	32.0 mmol
- potassium	40.0 mmol	32.0 mmol	24.0 mmol
- magnesium	6.7 mmol	5.3 mmol	4.0mmol
- calcium	3.3 mmol	2.7 mmol	2.0mmol
- phosphate[1]	18.0 mmol	14.0 mmol	11.0 mmol
- sulphate	6.7 mmol	5.3 mmol	
- chloride	78.0 mmol	62.0 mmol	4.0mmol
- acetate	65.0 mmol	52.0 mmol	47.0 mmol
			39.0 mmol
o Osmolality	approx. 830 mosm/kg water		
o Osmolarity	approx. 750 mosmol/l		
o pH	approx. 5.6		

[1] Contribution is from both Intralipid® and Vamin®

For the full list of excipients see section 6.1.

3 PHARMACEUTICAL FORM

Emulsion for infusion.

Kabiven Peripheral consists of a three chamber bag. The individual chambers contain glucose- and amino acid solutions, and fat emulsion, respectively. Glucose and amino acid solutions are clear and colourless or slightly yellow and the fat emulsion is white and homogenous.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Parenteral nutrition for patients and children above 2 years of age when oral or enteral nutrition is impossible, insufficient or contraindicated.

4.2 Posology and method of administration

The ability to eliminate fat and metabolise glucoseshould govern the dosage and infusion rate. See 4.4 "Special warning and precautions for use".

Posology
The dose should be individualised and the choice of bag size should be made with regard to the patient's clinical condition, body weight and nutritional requirements.

Adult patients
The nitrogen requirements for maintenance of body protein mass depend on the patient's condition (e.g. nutritional state and degree of catabolic stress). The requirements are 0.10-0.15 g nitrogen/kg b.w./day in the normal nutritional state. In patients with moderate to high metabolic stress with or without malnutrition, the requirements are in the range of 0.15-0.30 g nitrogen/kg b.w./day (1.0-2.0 g amino acid/kg b.w./day). The corresponding commonly accepted requirements are 2.0-6.0 g for glucose and 1.0-2.0 g for fat.

The total energy requirement depends on the patient's clinical condition and is often between 20-30 kcal/kg b.w./day. In obese patients the dose should be based on the estimated ideal weight.
Kabiven Peripheral is produced in three sizes intended for patients with moderately increased, basal or low nutritional requirements. To provide total parenteral nutrition, the addition of trace elements, vitamins and supplemental electrolytes may be required.

The dose range of 0.10-0.15g N/kg b.w./day (0.7-1.0 g amino acid/kg body weigh/day)and a total energy of 20-30 kcal body weight/day corresponds to approx. 27-40 ml Kabiven Peripheral/kg b.w./day.

Paediatric population
The ability to metabolise individual nutrients must determine the dosage.

In general the infusion for small children (2-10 years) should start with a low dose i.e. 14-28 ml/kg (corresponding to 0.49-0.98 g fat/kg/day, 0.34-0.67 g amino acids/kg/day and 0.95-1.9 g glucose/kg/day) and increased by 10-15 ml/kg/day up to maximum dosage of 40 ml/kg/day.

For children over 10 years of age the dosage for adults can be applied.
The use of Kabiven peripheral is not recommended in children under 2 years of age in whom the amino acid cysteine may be considered conditionally essential.

Infusion rate:
The maximum infusion rate for glucose is 0.25 g/kg b.w./h.
Amino acid dosage should not exceed 0.1 g/ kg b.w. /h.
Fat dosage should not provide more than 0.15 g/ kg b.w./h.

The infusion rate should not exceed 3.7 ml/kg b.w./h (corresponding to 0.25 g glucose, 0.09 g amino acids, 0.13 g fat per kg body weight). The recommended infusion period for individual bags of Kabiven Peripheral is 12-24 hours.

Maximum daily dose
40 ml/kg b.w./day. This is equal to one bag (largest size) to a 64 kg-patient and will provide 0.96 g amino acids/ kg b.w./day (0.16 g N/ kg b.w./day), 25 kcal/ kg b.w./day non-protein energy (2.7 g glucose/ kg b.w./day and 1.4 g fat/ kg b.w./day).
The maximum daily dose varies with the clinical condition of the patient and may even change from day to day**.**

Method of administration
Intravenous infusion into a peripheral or central vein. Infusion may be continued for as long as required by the patient's clinical condition.

In order to minimise the risk of thrombophlebitis for peripheral application, daily rotation of infusion site is recommended.

4.3 Contraindications

Hypersensitivity to egg-, soya- or peanut protein, to any of the active substances or to any of the excipients listed in section 6.1
Severe hyperlipaemia
Severe liver insufficiency
Severe blood coagulation disorders
Inborn errors of amino acid metabolism
Severe renal insufficiency without access to haemofiltration or dialysis
Acute shock
Hyperglycemia, which requires more than 6 units insulin/h
Pathologically elevated serum levels of any of the included electrolytes.
General contra-indications to infusion therapy: acute pulmonary oedema, hyper hydration and decompensated cardiac insufficiency and hypotonic dehydration
Haemophagocytotic syndrome
Unstable conditions (e.g. severe post-traumatic conditions, uncompensated diabetes, acute myocardial infarction, metabolic acidosis, severe sepsis and hyperosmolar coma)
Infants and children under 2 years of age.

4.4 Special warnings and precautions for use

The ability to eliminate fat should be monitored. It is recommended that this is done by measuring serum triglycerides after a fat-free period of 5-6 hours.
The serum concentration of triglycerides should not exceed 3 mmol/l during infusion.

The bag size, specially the volume and the quantitative composition, should be carefully chosen. These volumes should be adjusted according to the hydration and nutritional status of the children. One reconstituted bag is for single use.

Disturbances of the electrolyte and fluid balance (e.g. abnormally high or low serum levels of the electrolytes) should be corrected before starting the infusion.

Special clinical monitoring is required at the beginning of any intravenous infusion. Should any abnormal sign occur, the infusion must be stopped. Since an increased risk of infection is associated with the use of any central vein, strict aseptic precautions should be taken to avoid any contamination during catheter insertion and manipulation.

Kabiven Peripheral should be given with caution in conditions of impaired lipid metabolism which may occur in patients with renal insufficiency, uncompensated diabetes mellitus, pancreatitis, impaired liver function, hypothyroidism (with hypertriglyceridaemia) or sepsis. If Kabiven Peripheral is given to patients with these conditions, close monitoring of serum triglyceride concentrations is mandatory.

Serum glucose, electrolytes and osmolarity as well as fluid balance, acid-base status and liver enzyme tests should be regularly monitored.

Blood cell count and coagulation should be monitored when fat is given for a longer period.

In patients with renal insufficiency, the phosphate and potassium intake should be carefully controlled to prevent hyperphosphataemia and hyperkalemia.

The amount of supplemental electrolytes should be determined by regular monitoring taking into consideration the clinical condition of the patient.

This emulsion is free of vitamins and trace-elements.
The addition of trace elements and vitamins is always required.
Parenteral nutrition should be given with caution to patients with metabolic acidosis (e.g. lactic acidosis), increased serum osmolarity or those in need of fluid resuscitation.
Kabiven Peripheral should be given with caution to patients with a tendency towards electrolyte retention.

Any sign or symptom of anaphylactic reaction necessitates immediate interruption of the infusion.

The fat content of Kabiven Peripheral may interfere with certain laboratory measurements (e.g. bilirubin, lactate dehydrogenase, oxygen saturation, Hb) if blood is sampled before fat has been adequately cleared from the bloodstream. Fat is cleared after a fat-free interval of 5-6 hours in most patients.

This medicinal product contains soya-bean oil and egg phospholipids, which may rarely cause allergic reactions. Cross allergic reaction has been observed between soya-bean and peanut.

Intravenous infusion of amino acids may be accompanied by increased urinary excretion of trace elements, particularly zinc. Additional supplements of trace elements may be required in patients requiring long-term intravenous nutrition.

In malnourished patients, initiation of parenteral nutrition can precipitate fluid shifts resulting in pulmonary oedema and congestive heart failure. In addition, decreases in the serum concentrations of potassium, phosphorus, magnesium and water soluble vitamins may occur within 24 to 48 hours. Careful and slow initiation of parenteral nutrition is recommended together with close monitoring and appropriate adjustments of fluid, electrolytes, minerals and vitamins.

Kabiven Peripheral should not be given simultaneously with blood or blood products in the same infusion set.

In patients with hyperglycaemia, administration of exogenous insulin might be necessary.

Peripheral infusion
As with all hypertonic solutions, thrombophlebitis may occur if peripheral veins are used for infusions. Several factors contribute to the incidence of thrombophlebitis. These include the type of cannula used and its diameter and length, the duration of infusion, pH and osmolality of infusates, infection and the number of manipulations. It is recommended that venous access sites for TPN should not be used for other intravenous additives or solutions.

4.5 Interaction with other medicinal products and other forms of interactions

Heparin given in clinical doses causes a transient release of lipoprotein lipase into the circulation. This may result initially in increased plasma lipolysis followed by a transient decrease in triglyceride clearance.

Other drugs, such as insulin, may influence lipase activity but there is no evidence to suggest that this adversely effects therapeutic value.

Soybean oil has a natural content of vitamin K1 which could effect coagulation particulary in patients receiving coumarin derivates. In practice this is uncommon but close monitoring of coagulation is advised for patients receiving these drugs. There are no clinical data to show that any of the above mentioned interactions are of defininte clinical relevance.

4.6 Fertility, pregnancy and lactation

No specific studies have been performed to assess the safety of Kabiven Peripheral in pregnancy and lactation. The prescriber should consider the benefit/risk relationship before administering Kabiven Peripheral to pregnant or breast feeding women.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

	Common (≥ 1/100 to < 1/10)	*Uncommon (≥ 1/1000, < 1/100)*	*Very rare (< 1/10000)*
Blood and lymphatic system disorders			Haemolysis, reticulocytosis
Immune system disorders			Hypersensitivity reactions (e.g. anaphylactic reaction, skin rash, urticaria)

Nervous system disorders		Headache	
Vascular disorders	Thrombophlebitis		Hypotension, hypertension
Respiratory, thoracic and mediastinal disorders			Tachypnoea
Gastrointestinal disorders		Abdominal pain, nausea, vomiting	
Reproductive system and breast disorders			Priapism
General disorders and administration site conditions	Rise in body temperature	Chills, tiredness	
Investigations		Increase in plasma levels of liver enzymes	

As with all hypertonic solutions for infusion, thrombophlebitis may occur if peripheral veins are used.

Fat overload syndrome
An impaired capacity to eliminate fat may lead to the fat overload syndrome. This may occur as a result of overdosage, but also at recommended rates of infusion, in association with a sudden change in the patient's clinical condition resulting in severe renal or hepatic impairment.

The fat overload syndrome is characterised by hyperlipidaemia, fever, hepato- splenomegaly, anaemia, leucopenia, thrombocytopenia, coagulopathies and coma. These changes are invariably reversible on discontinuation of the fat infusion.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system

For Ireland:
You can report side effects directly via:

HPRA Pharmacovigilance,
Earlsfort Terrace,
IRL - Dublin 2;
Tel: +353 1 6764971;
Fax: +353 1 6762517.
Website: www.hpra.ie;
E-mail: medsafety@hpra.ie

4.9 Overdose

See section 4.8, "Fat overload syndrome".
Nausea, vomiting and sweating have been observed during infusion of amino acids at rates exceeding the recommended maximum rate.

If symptoms of overdose occur, the infusion should be slowed down or discontinued.
Additionally, overdose might cause fluid overload, electrolyte imbalances, hyperglycaemia, and hyperosmolality.

In some rare serious cases, haemodialysis, haemofiltration or haemo-diafiltration may be necessary.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Solution for parenteral nutrition.
ATC code: B05BA10

FAT EMULSION
Intralipid, the fat emulsion used in Kabiven Peripheral, provides essential and non-essential long-chain fatty acids for energy metabolism and the structural integrity of cell membranes.

Intralipid in the recommended dosage does not cause haemodynamic changes. No clinically significant changes in pulmonary function have been described when Intralipid is used at appropriate infusion rates. The transient increase in liver enzymes observed in some patients on parenteral nutrition are reversible and disappear when parenteral nutrition is discontinued. Similar changes are also seen in parenteral nutrition without fat emulsions.

AMINO ACIDS AND ELECTROLYTES

Amino acids are constituents of protein in ordinary food. They are utilised for tissue protein synthesis and any surplus is channeled towards gluconeogenesis. Infusions of amino acids are associated with small increases in metabolic rate and thermogenesis.

GLUCOSE

Glucose has no pharmacodynamic effects apart from contributing to normal homeostasis.

5.2 Pharmacokinetic properties

FAT EMULSION
Intralipid has biological properties similar to those of endogenous chylomicrons. Unlike chylomicrons, Intralipid does not contain cholesterol esters or apolipoproteins, while its phospholipid content is significantly higher.

Intralipid is eliminated from the circulation by a pathway similar to that of endogenous chylomicrons. The exogenous fat particle is primarily hydrolysed in the circulation and taken up by LDL receptors both peripherally and in the liver. The elimination rate is determined by the composition of the fat particles, the patient's nutritional and clinical status, and the rate of infusion. In healthy volunteers, the maximum clearance rate of Intralipid after fasting overnight is equivalent to 3.8 $\pm$1.5 g of triglycerides per kg b.w. per 24 hours.

Both the elimination and the oxidation rates are dependent on the patients clinical condition; elimination is faster and oxidation rates increased in septic states and following trauma, while patients with renal failure or hypertriglyceridaemia have lower rates of elimination and oxidation.

AMINO ACIDS AND ELECTROLYTES
The principal pharmacokinetic properties of the infused amino acids and electrolytes are essentially the same as for amino acids and electrolytes supplied by ordinary food. However, the amino acids of dietary protein first enter the portal vein and then the systemic circulation, while intravenously infused amino acids reach the systemic circulation directly.

GLUCOSE
The pharmacokinetic properties of infused glucose are essentially the same as those of glucose supplied by ordinary food.

5.3 Preclinical safety data

Preclinical safety studies with Kabiven Peripheral have not been performed. However, preclinical safety studies with Intralipid, Vamin based amino acid solutions, electrolytes and glucose, either individually or mixed in various compositions and concentrations, confirm satisfactory tolerance with minimal adverse effects.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Purified egg phospholipids
Glycerol
Sodium Hydroxide (for pH adjustment)
Acetic acid, glacial (for pH adjustment)
Water for injections

6.2 Incompatibilities

Kabiven Peripheral may only be mixed with other medicinal products for which compatibility has been documented. *See section 6.6 Instruction for use/handling.*

6.3 Shelf life

2 years in the overpouch**.**

SHELF LIFE AFTER MIXING
After breaking the seals, chemical and physical in-use stability of the mixed three chamber bag has been demonstrated for 24 hours at 25°C.

6.4 Special precautions for storage

Do not store above 25°C. Store in overpouch. Do not freeze.

AFTER MIXING WITH ADDITIVES
After opening the peelable seals and mixing of the three solutions, additions can be made via medication port.
From a microbiological point of view the product should be used immediately when addition have been made. If not used immediately, the in-use storage time and conditions prior to use are the responsibility of the user and should normally not be longer than 24 hours at 2-8°C. If storage can not be avoided and provided that additions are made under controlled and validated aseptic conditions the mixed emulsion may be stored up to 6 days at 2-8°C before being used. After removal from storage at 2-8°C, the admixture should be infused within 24 hours.

6.5 Nature and contents of container

The container consists of a multichamber inner bag and an overpouch. The inner bag is separated into three chambers by peelable seals. An oxygen absorber is placed between the inner bag and the overpouch.

The inner bag is made of a multilayer polymer film, Biofine.

The Biofine inner bag film consists of poly(propylene-co-ethylene), synthetic rubber poly[styrene-block-(butylene-co-ethylene)] (SEBS) and synthetic rubber poly(styrene-block-isoprene) (SIS). The infusion and additive ports are made of polypropylene and synthetic rubber poly[styrene-block-(butylene-co-ethylene)] (SEBS) equipped with synthetic polyisoprene (latex-free) stoppers. The blind port, which is only used during manufacturing, is made of polypropylene equipped with a synthetic polyisoprene (latex-free) stopper.

Pack sizes:

1 x 1440 ml, 4 x 1440 ml
1 x 1920 ml, 4 x 1920 ml
1 x 2400 ml, 3 x 2400 ml

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

For single use only.

Do not use if package is damaged. The contents of the three separate chambers have to be mixed before use.

After separation of the peelable seals the bag should be inverted on a number of occasions to ensure a homogenous mixture.

Use only if the amino acids and glucose solutions are clear and colourless or slightly yellow and if the fat emulsion is white and homogenous.

COMPATIBILITY

Additives
Only medicinal or nutritional solutions for which compatibility has been documented may be added to Kabiven Peripheral.

Addition should be made aseptically.

Mixing data are delivered upon request.

Any mixture remaining after infusion must be discarded.

7 MARKETING AUTHORISATION HOLDER

Fresenius Kabi Deutschland GmbH
Else-Kroener Strasse 1
Bad Homburg v.d.H 61352
Germany

8 MARKETING AUTHORISATION NUMBER

PA2059/045/004

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 28 July 2006

Date of last renewal: 12 March 2009

10 DATE OF REVISION OF THE TEXT

November 2019