Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Kabiven emulsion for infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

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

	2566 ml	**2053 ml**	**1540 ml**	**1026 ml**
Glucose (Glucose 19%)	1316 ml	1053 ml	790 ml	526 ml
Amino acids and electrolytes (Vamin 18 Novum)	750 ml	600 ml	450 ml	300 ml
Fat emulsion (Intralipid 20%)	500 ml	400 ml	300 ml	200 ml

This corresponds to the following total compositions:

Active ingredients	**2566 ml**	**2053 ml**	**1540 ml**	**1026 ml**
Purified soybean oil	100 g	80 g	60 g	40 g
Glucose monohydrate corresponding to	275 g	220 g	165 g	110 g
Glucose (anhydrous)	250 g	200 g	150 g	100 g
Alanine	12.0 g	9.6 g	7.2 g	4.8 g
Arginine	8.5 g	6.8 g	5.1g	3.4 g
Aspartic acid	2.6 g	2.0 g	1.5 g	1.0 g
Glutamic acid	4.2 g	3.4 g	2.5 g	1.7 g
Glycine	5.9 g	4.7 g	3.6 g	2.4 g
Histidine	5.1 g	4.1 g	3.1 g	2.0 g
Isoleucine	4.2 g	3.4 g	2.5 g	1.7 g
Leucine	5.9 g	4.7 g	3.6 g	2.4 g
Lysine hydrochloride	8.5 g	6.8 g	5.1 g	3.4 g
corresponding to Lysine	6.8 g	5.4 g	4.1 g	2.7 g
Methionine	4.2 g	3.4 g	2.5 g	1.7 g
Phenylalanine	5.9 g	4.7 g	3.6 g	2.4 g
Proline	5.1 g	4.1 g	3.1 g	2.0 g
Serine	3.4 g	2.7 g	2.0 g	1.4 g
Threonine	4.2 g	3.4 g	2.5 g	1.7 g
Tryptophan	1.4 g	1.1 g	0.86 g	0.57 g
Tyrosine	0.17 g	0.14 g	0.10 g	0.07 g
Valine	5.5 g	4.4 g	3.3 g	2.2 g

Active ingredients	**2566 ml**	**2053 ml**	**1540 ml**	**1026 ml**
Calcium chloride 2 H_2O	0.74 g	0.59 g	0.44 g	0.29 g
corresponding to Calcium chloride	0.56 g	0.44 g	0.33 g	0.22 g
sodium glycerophosphate (anhydrous)	3.8 g	3.0 g	2.3 g	1.5 g
Magnesium sulphate 7H_2O	2.5 g	2.0 g	1.5 g	0.99 g
corresponding to Magnesium sulphate	1.2 g	0.96 g	0.72 g	0.48 g
Potassium chloride	4.5 g	3.6 g	2.7 g	1.8 g
Sodium acetate 3 H_20	6.1 g	4.9 g	3.7 g	2.5 g
corresponding to Sodium acetate	3.7 g	2.9 g	2.2 g	1.5 g

Corresponding to

	2566 ml	**2053 ml**	**1540 ml**	**1026 ml**
o Amino acids	85 g	68 g	51g	34 g
o Nitrogen	13.5 g	10.8 g	8.1 g	5.4 g
o Fat	100 g	80 g	60 g	40 g
o Carbohydrates				
- Glucose (dextrose)	250 g	200 g	150 g	100 g
o Energy content				
- total	2300 kcal	1900 kcal	1400 kcal	900 kcal
- non protein	2000 kcal	1600 kcal	1200 kcal	800 kcal
o Electrolytes				
- sodium	80 mmol	64 mmol	48 mmol	32 mmol
- potassium	60 mmol	48 mmol	36 mmol	24 mmol
- magnesium	10 mmol	8 mmol	6 mmol	4 mmol
- calcium	5 mmol	4 mmol	3 mmol	2 mmol
- phosphate[1]	25 mmol	20 mmol	15 mmol	10 mmol
- sulphate	10 mmol	8 mmol	6 mmol	4 mmol
- chloride	116 mmol	93 mmol	70 mmol	46 mmol
- acetate	97 mmol	78 mmol	58 mmol	39 mmol
o Osmolality	approx. 1230 mosm/kg water			
o Osmolarity	approx. 1060 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 consists of a three chamber bag and an overpouch. An oxygen absorber is placed between the inner bag and the overpouch. The inner bag is separated into three chambers by peelable seals. The individual chambers contain glucose- and amino acid solutions, and fat emulsion, respectively. Glucose and amino acid solutions are clear solutions and fat emulsion is white.

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 warnings 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 body weight/day in the normal nutritional state or in conditions with mild metabolic stress. 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 body weight/day (1.0-2.0 g amino acid/kg body weight/day). The corresponding commonly accepted requirements are 2.0-6.0 g for glucose and 1.0-2.0 g for fat.

The dose range of 0.10 - 0.20 g nitrogen/kg body weight/day (0.7-1.3 g amino acid/kg body weight/day) which covers the need of the majority of the patients.Thiscorresponds to 19 ml - 38 ml Kabiven/kg body weight/day. For a 70-kg-patient this is equivalent to 1330 ml - 2660 ml Kabiven per day.

The total energy requirement depends on the patient's clinical condition and is most often between 25 - 35 kcal/kg body weight/day. In obese patients the dose should be based on the estimated ideal weight.

Kabiven is produced in four sizes intended for patients with high, moderately increased, basal, or low nutritional requirements. To provide total parenteral nutrition, trace elements and vitamins should be given additionally.

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. 12.5-25 ml/kg (corresponding to 0.49-0.98 g fat/kg/day, 0.41-0.83 g amino acids/kg/day and 1.2-2.4 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 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/h.
Amino acid dosage should not exceed 0.1 g/kg/h.
Fat dosage should not provide more than 0.15 g/kg/h.

The infusion rate should not exceed 2.6 ml/kg body weight/hour (corresponding to 0.25 g glucose, 0.09 g amino acid and 0.1 g fat/kg body weight). The recommended infusion period is 12-24 hours.

Maximum daily dose
40 ml/kg bw/day. This is equal to one bag (largest size) to a 64 kg-patient and will provide 1.3 g amino acids/kg/day (0.21 g N/kg/day), 31 kcal/kg/day non-protein energy (3.9 g glucose/kg/day and 1.6 g fat/kg/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 only into a central vein. Infusion may be continued for as long as required by the patient's clinical condition.

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 hemofiltration or dialysis
Acute shock
Hyperglycemia, which requires more than 6 units insulin/h
Pathologically elevated serum levels of any of the included electrolytes.
General contraindications to infusion therapy: acute pulmonary edema, hyperhydration, decompensated cardiac insufficiency and hypotonic dehydration
Hemophagocytotic 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 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 hypertriglyceridemia) and sepsis. If Kabiven is given to patients with these conditions, close monitoring of serum triglycerides is mandatory.

Serum glucose, electrolytes and osmolarity as well as fluid balance, acid-base status and liver enzyme tests (alkaline phosphatase, ALT, AST)should be 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 potassiumintake should be carefully controlled to prevent hyperphosphatemia and hyperkalaemia**.**

The amount of individual electrolytes to be added is governed by the clinical condition of the patient and by frequent monitoring of serum levels.

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 in metabolic acidosis, lactic acidosis, insufficient cellular oxygen supply and increased serum osmolarity.

Kabiven should be given with caution to patients with a tendency towards electrolyte retention.

Any sign or symptom of anaphylactic reaction (such as fever, shivering, rash or dyspnoea) should lead to immediate interruption of the infusion.

The fat content of Kabiven 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 is accompanied by increased urinary excretion of the trace elements copper and, in particular, zinc. This should be considered in the dosing of trace elements, especially during long-term intravenous nutrition.

In malnourished patients, initiation of parenteral nutrition can precipitate fluid shifts resulting in pulmonary oedema and congestive heart failure as well as a decrease in the serum concentration of potassium, phosphorus, magnesium and water soluble vitamins. These changes can occur within 24 to 48 hours, therefore careful and slow initiation of parenteral nutrition is recommended together with close monitoring and appropriate adjustments of fluid, electrolytes, minerals and vitamins.

Kabiven should not be given simultaneously with blood in the same infusion set due to the risk of pseudoagglutination.

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

4.5 Interaction with other medicinal products and other forms of interaction

Some drugs, like insulin, may interfere with the body's lipase system. This kind of interaction seems, however, to be of only limited clinical importance.

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.

Soybean oil has a natural content of vitamin K1. This may interfere with the therapeutic effect of coumarin derivatives which should be closely monitored in patients treated with such drugs.

There are no clinical data to show that any of above mentioned interactions are of definite Clinical relevance.

4.6 Fertility, pregnancy and lactation

No specific studies have been performed to assess the safety of Kabiven in pregnancy and lactation. The prescriber should consider the benefit/risk relationship before administering Kabiven 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 to < 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			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 Intralipid (the fat component in Kabiven)may lead to the fat overload syndrome as a result of overdosage, but also at recommended rates of infusion in association with a sudden change in the patient's clinical condition, such as renal function impairment or infection.

The fat overload syndrome is characterised by hyperlipaemia, fever, fat infiltration, hepatomegaly, splenomegaly, anaemia, leucopenia, thrombocytopenia, blood coagulation disorders and coma. All symptoms are usually reversible if the infusion is discontinued.

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 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, hyperglycemia, 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, 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 properly. The transient increase in liver enzymes seen in some patients on parenteral nutrition is reversible and disappears when parenteral nutrition is discontinued. Similar changes are also seen in parenteral nutrition without fat emulsions.

AMINO ACIDS AND ELECTROLYTES
The amino acids, constituents of protein in ordinary food, are utilised for tissue protein synthesis and any surplus is channelled to a number of metabolic pathways.
Studies have shown a thermogenic effect of amino acid infusion.

GLUCOSE
Glucose should have no pharmacodynamic effects apart from contributing to maintain or replete the normal nutritional status.

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 via a pathway similar to that of endogenous chylomicrons, at least early on in the catabolism. The exogenous fat particle is primarily hydrolysed in the circulation and taken up by LDL receptors peripherally and by the liver. The elimination rate is determined by the composition of the fat particles, the nutritional status, the disease 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 body weight per 24 hours.

Both the elimination and the oxidation rates are dependent on the patient's clinical condition; elimination is faster and utilisation is increased in postoperative patients and in trauma, while patients with renal failure and hypertriglyceridaemia show lower utilisation of exogenous fat emulsions.

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 have not been performed. However, preclinical safety studies with Intralipid as well as with amino acid, electrolytes and glucose solutions of various compositions and concentrations demonstrate a good tolerance.

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

6.3 Shelf life

2yearsin the overpouch.

SHELF LIFE AFTER MIXING THE CHAMBERS OF THE BAG
After breaking the seals, chemical and physical in-use stability of the mixed three chamber bag has been demonstrated for 48 hours at 20- 25°C.

including duration of administration. From a microbiological point of view the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2-8°C, unless mixing has taken place in controlled and validated aseptic conditions.

SHELF LIFE AFTER MIXING WITH ADDITIVES
After opening the peelable seals and mixing of the three solutions, additions can be made via medication port.
Physico-chemical in-use stability of the mixed three chamber bag with additives (see section 6.6) has been demonstrated for up to 8 days, i.e., 6 days at 2-8°C followed by 48 hours at 20-25°C, or with Omegaven addition for 48 hours at 20-25°C, including duration of administration. From a microbiological point of view, the product should be used immediately when additions 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, unless addition of supplements has taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage

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

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, i.e. 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-blockisoprene) (SIS). The infusion and additive ports are made of polypropylene and synthetic rubber poly[styrene-block-(butene-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 1026 ml, 4 x 1026 ml

1 x 1540 ml, 4 x 1540 ml
1 x 2053 ml, 4 x 2053 ml
1 x 2566 ml, 3 x 2566 ml

Not all pack sizes may be marketed

6.6 Special precautions for disposal and other handling

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

To ensure a homogenous admixture, the bag should be inverted a couple of times immediately before the infusion.
Use only if the amino acids and glucose solutions are clear colourless or slightly yellow and if the fat emulsion is white and homogenous.

COMPATIBILITY

Compatibility data are available with the named branded products Dipeptiven, Omegaven, Addamel N/Addaven, Glycophos, Addiphos, Vitalipid N Adult/Infant and Soluvit N in defined amounts and generics of electrolytes in defined concentrations. When making electrolyte additions, the amounts already present in the bag should be taken into account to meet the clinical needs of the patient. Generated data supports additions to the activated bag according to the summary tables below:
Compatibility range stable for 8 days, i.e., 6 days storage at 2-8°C followed by 48 hours at 20-25°C

	Units	**Maximal total contents**			
Kabiven bag size	ml	1026	1540	2053	2566
Additive		**Volume**			
Dipeptiven	ml	0 - 200	0 - 300	0 - 300	0 - 300
Addaven/Addamel N	ml	0 - 10	0 - 10	0 - 20	0 - 20
Soluvit N	vial	0 - 1	0 - 1	0 - 2	0 - 2
Vitalipid N Adult/Infant	ml	0 - 10	0 - 10	0 - 20	0 - 20
Electrolyte limits[1]		**Amount per bag**			
Sodium	mmol	≤ 154	≤ 231	≤ 308	≤ 385
Potassium	mmol	≤ 154	≤ 231	≤ 308	≤ 385
Calcium	mmol	≤ 5	≤ 7.5	≤ 10	≤ 12.5
Magnesium	mmol	≤ 5	≤ 7.5	≤ 10	≤ 12.5
Phosphate inorganic (Addiphos) OR Phosphate organic (Glycophos)	mmol	≤ 15	≤ 22.5	≤ 30	≤ 37.5

1. includes amounts from all products

Compatibility range stable with Omegaven for 48 hours at 20-25°C

	Units	**Maximal total contents**			
Kabiven bag size	ml	1026	1540	2053	2566
Additive		**Volume**			
Dipeptiven	ml	0 - 100	0 - 200	0 - 300	0 - 300
Omegaven	ml	0-50	0 - 100	0 - 100	0 - 100
Addaven/Addamel N	ml	0 - 10	0 - 10	0 - 10	0 - 10
Soluvit N	vial	0 - 1	0 - 1	0 - 1	0 - 1
Vitalipid N Adult/Infant	ml	0 - 10	0 - 10	0 - 10	0 - 10
Electrolyte limits[1]		**Amount per bag**			
Sodium	mmol	≤ 150	≤ 225	≤ 300	≤ 375
Potassium	mmol	≤ 150	≤ 225	≤ 300	≤ 375
Calcium	mmol	≤ 5	≤ 7.5	≤ 10	≤ 12.5
Magnesium	mmol	≤ 5	≤ 7.5	≤ 10	≤ 12.5
Phosphate inorganic (Addiphos)	mmol	≤ 15	≤ 22.5	≤ 30	≤ 37.5

OR Phosphate organic (Glycophos)					

1. includes amounts from all products

Note: These tables are intended to indicate compatibility. They are not a dosing guideline.

For branded products, before prescribing refer to national approved prescribing information.

Compatibility with further additives and the storage time of different admixtures will be available upon request.

Additions should be made aseptically

Any mixture remaining after infusion must be discarded.

Any unused medicinal product or waste material should be disposed in accordance with local requirement.

7 MARKETING AUTHORISATION HOLDER

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

8 MARKETING AUTHORISATION NUMBER

PA2059/045/003

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

December 2023