

DATA SHEET

NAME OF MEDICINE:

KABIVEN® G19%

PRESENTATION:

Kabiven G19% 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, amino acid solutions, and fat emulsion, respectively. The glucose and amino acid solutions are clear solutions while the fat emulsion is white.

Each bag contains the following different volumes depending on the four pack sizes.

	2566 mL	2053 mL	1540 mL	1026 mL
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 compositions.

Active Ingredients	2566 mL	2053 mL	1540 mL	1026 mL
Soya Oil (g)	100	80	60	40
Glucose monohydrate (g)	275	220	165	110
Corresponding to Glucose (anhydrous) (g)	250	200	150	100
Alanine (g)	12.0	9.6	5.1	3.4
Arginine (g)	8.5	6.8	5.1	3.4
Aspartic acid (g)	2.6	2.0	1.5	1.0
Glutamic acid (g)	4.2	3.4	2.5	1.7
Glycine (g)	5.9	4.7	3.6	2.4
Histidine (g)	5.1	4.1	3.1	2.0
Isoleucine (g)	4.2	3.4	2.5	1.7
Leucine (g)	5.9	4.7	3.6	2.4
Lysine hydrochloride (g)	8.5	6.8	5.1	3.4
Corresponding to Lysine (g)	6.8	5.4	4.1	2.7
Methionine (g)	4.2	3.4	2.5	1.7
Phenylalanine (g)	5.9	4.7	3.6	2.4
Proline (g)	5.1	4.1	3.1	2.0
Serine (g)	3.4	2.7	2.0	1.4
Threonine (g)	4.2	3.4	2.5	1.7
Tryptophan (g)	1.4	1.1	0.86	0.57
Tyrosine (g)	0.17	0.14	0.10	0.07

Valine (g)	5.5	4.4	3.3	2.2
Active Ingredients	2566	2053	1540	1026
	mL	mL	mL	mL
Calcium chloride.2H ₂ O (g)	0.74	0.59	0.44	0.29
Corresponding to Calcium chloride (g)	0.56	0.44	0.33	0.22
Potassium chloride (g)	4.5	3.6	2.7	1.8
Magnesium sulphate.7H ₂ O (g)	2.5	2.0	1.5	0.99
Magnesium sulphate (g)	1.2	0.96	0.72	0.48
Sodium acetate.3H ₂ O (g)	6.1	4.9	3.7	2.5
Corresponding to Sodium acetate (g)	3.7	2.9	2.2	1.5
Sodium glycerophosphate (anhydrous) (g)	3.8	3.0	2.3	1.5
Corresponding to				
	2566	2053	1540	1026
	mL	mL	mL	mL
• Amino acids (g)	85	68	51	34
• Nitrogen (g)	13.5	10.8	8.1	5.4
• Fat (g)	100	80	60	40
• Carbohydrates – glucose (dextrose) (g)	250	200	150	100
• Energy content				
– Total (kcal)	2300	1900	1400	900
– None protein (kcal)	2000	1600	1200	800
• Electrolytes				
– sodium (mmol)	80	64	48	32
– potassium (mmol)	60	48	36	24
–magnesium (mmol)	10	8	6	4
– calcium (mmol)	5	4	3	2
– phosphate (mmol)	25	20	15	10
– sulfate (mmol)	10	8	6	4
– chloride (mmol)	116	93	70	46
– acetate (mmol)	97	78	58	39
• Osmolality	Approx 1230 mOsm/kg water			
• Osmolarity	Approx. 1060 mOsm/L			
• pH	Approx 5.6			

Kabiven G19% also contains egg lecithin, glycerol, sodium hydroxide, acetic acid, glacial and water for injections.

USES

Actions:

Fat emulsion

Intralipid, the fat emulsion used in Kabiven G19% provides essential and non-essential long chain fatty acids for energy metabolism and the structural integrity of cell membranes.

Intralipid in the recommended dosage dose 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.

Pharmacokinetics

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 the 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 ± 1.5 g of triglyceride 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 principle 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.

INDICATIONS

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

DOSAGE AND ADMINISTRATION

The ability to eliminate fat and metabolise glucose should govern the dosage and infusion rate. See "Warnings and Precautions".

Dosage

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 nitrogen/kg body weight (b.w.)/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 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 dose range of 0.10-0.20 g nitrogen/kg b.w./day (0.7-1.3 g amino acid/kg b.w./day) which covers the need of the majority of the patients. This corresponds to 19 mL – 38 mL Kabiven/kg b.w./day. For a 70 kg patient this is equivalent to 1330 mL to 2660 mL Kabiven G19% per day.

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

Kabiven G19% is produced in four sizes intended with high, moderately increased, basal, or low nutritional requirements. To provide total parenteral nutrition, trace elements and vitamins should be given additionally.

Children

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 a 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 G19% 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 b.w./hour (corresponding to 0.25 g glucose, 0.09 g amino acid and 0.1 g fat/kg b.w.). The recommended infusion period 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 1.3 g amino acids/kg b.w./day (0.21 g N/kg b.w./day), 31 kcal/kg b.w./day non-protein energy (3.9 g glucose/kg b.w./day and 1.6 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 and duration of administration

Intravenous infusion only into a central vein. Infusion may be continued for as long as required by the patient's clinical condition.

CONTRAINDICATIONS

- Hypersensitivity to egg-, soya- or peanut protein or to any of the ingredients
- 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
- Hyperglycaemia, 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 oedema, hyperhydration, 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)
- Due to composition, Kabiven G19% is not suitable for use in new-borns or infants under 2 years of age.

WARNINGS AND PRECAUTIONS

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 3mmol/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 G19% should be given with caution in conditions of impaired lipid metabolism, such as in renal insufficiency, uncompensated diabetes mellitus, pancreatitis, impaired liver function, hypothyroidism (with hypertriglyceridaemia) and sepsis. If Kabiven G19% 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 potassium intake should be carefully controlled to prevent hyperphosphataemia 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. For vitamin supplementation, paediatric formulations are recommended to be used.

Parenteral nutrition should be given with caution in metabolic acidosis, lactic acidosis, insufficient cellular oxygen supply and increased serum osmolarity.

Kabiven G19% 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 G19% may interfere with certain laboratory measurements (e.g. bilirubin, lactate dehydrogenase, oxygen saturation, and haemoglobin) 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.

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 G19% 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.

Kabiven G19% contains soya oil and egg lecithin which may rarely cause allergic reactions. Cross allergic reaction has been observed between soya-bean and peanut.

Use in pregnancy (Category B2) and lactation

No specific studies have been performed to assess the safety of Kabiven G19% in pregnancy and lactation. The prescriber should consider the benefit/risk relationship before administering Kabiven G19% to pregnant or breast feeding women.

Effects on ability to drive and use machines

Not applicable

ADVERSE EFFECTS

Intralipid may cause a rise in body temperature (incidence < 3%) and, less frequently, shivering, chills and nausea/vomiting (incidence < 1%). Transient increases in liver enzymes during intravenous nutrition have also been reported.

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

Reports of other undesirable effects in conjunction with Intralipid infusions are extremely rare; less than one adverse event per million infusions. Hypersensitivity reactions (anaphylactic reaction, skin rash, urticaria), respiratory symptoms (e.g. tachypnoea) and hyper/hypotension have been described. Haemolysis, reticulocytosis, abdominal pain, headache, tiredness and priapism have been reported.

Fat overload syndrome

An impaired capacity to eliminate fat may lead to the fat overload syndrome. This may occur as a result of overdosages, 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 hyperlipaemia, fever, fat infiltration, hepatomegaly, splenomegaly, anaemia, leucopenia, thrombocytopenia, blood coagulation disorders and coma. These changes are invariably reversible on discontinuation of the fat infusion.

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 medicines, like insulin, may influence lipase activity but there is no evidence to suggest that this adversely affects therapeutic value.

Soya 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 medicines.

There are no clinical data to show that any of the above listed interactions are of definite clinical relevance.

OVERDOSAGE

See "Fat overload syndrome" under "Adverse Reactions".

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.

PHARMACEUTICAL PRECAUTIONS

Store below 25°C. Store in overpouches. Do not freeze.

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.

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.

For single use only.

Do not use if package is damaged. Kabiven G19% should only be mixed and used if the solutions are clear and colourless or slightly yellow and if the emulsion is white and homogenous.

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.

Compatibility

Additives

Only medicinal or nutritional solutions for which compatibility has been documented may be added to Kabiven G19%.

Additions should be made aseptically.

The standard recommendation is given in the following tables.

Table 1

Kabiven G19% added with the following additives will be stable for up to 6 days stored at 2° to 8°C plus 48 hours stored at 20° to 25°C.

<u>Additions</u>	<u>2566 mL</u>	<u>2053 mL</u>	<u>1540 mL</u>	<u>1026 mL</u>
	<i>Up to a total of:</i>			
Soluvit N	1 vial	1 vial	1 vial	1 vial
Vitalipid N Adult	10 mL	10 mL	10 mL	10 mL
Addamel N	10mL	10mL	10mL	10mL
Dipeptiven	300mL	300mL	200mL	100mL
	<i>Up to a total of:</i>			
Sodium	385 mmol	308 mmol	231 mmol	154 mmol
Potassium	385 mmol	308 mmol	231 mmol	154 mmol
Magnesium	13 mmol	10 mmol	8 mmol	5 mmol
Calcium	13 mmol	10 mmol	8 mmol	5 mmol
Phosphate	38 mmol	31 mmol	23 mmol	15 mmol

Table 2

With the addition of the following amounts of Omegaven, the mixture will only be stable for up to 48 hours stored at 20° to 25°C.

<u>Additions</u>	<u>2566 mL</u>	<u>2053 mL</u>	<u>1540 mL</u>	<u>1026 mL</u>
	<i>Up to a total of:</i>			
Omegaven	100mL	100mL	100mL	50mL

Any mixture remaining after infusion must be discarded.

MEDICINE CLASSIFICATION

General Sale Medicine

PACKAGE QUANTITIES

Kabiven G19% is available in the following pack sizes:

Excel bags

1 x 1026ml, 4 x 1026ml

1 x 1540ml, 4 x 1540ml

1 x 2053ml, 2 x 2053ml
1 x 2566ml, 2 x 2566ml

Biofine bags

1 x 1026ml, 4 x 1026ml
1 x 1540ml, 4 x 1540ml
1 x 2053ml, 4 x 2053ml
1 x 2566ml, 3 x 2566ml

FURTHER INFORMATION

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, alternatively Excel or Biofine.

The **Excel** inner bag film consists of three layers. The inner layer consists of poly(propylene/ethylene) copolymer and styrene/ethylene/butylene/styrene thermoplastic elastomer (SEBS). The middle layer consists of SEBS and the outer layer consists of copolyester-ether. The infusion port is equipped with a polyolefine cap. The additive port is equipped with a synthetic polyisoprene (latex-free) stopper.

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.

NAME AND ADDRESS

Fresenius Kabi New Zealand Limited
60 Pavilion Drive
Airport Oaks, Auckland 2022
New Zealand
Freecall: 0800 144 892

DATE OF PREPARATION

23rd March, 2010