Kabiven™

Emulsion for infusion

Presentation
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.

Kabiven is available in four sizes. The volumes of the components (Glucose 19%, Vamin 18 and Intralipid 20%) are the following:

	2566 ml	2053 ml	1540 ml	1026 ml
Glucose 19%	1316 ml	1053 ml	790 ml	526 ml
Vamin 18 Novum	750 ml	600 ml	450 ml	300 ml
Intralipid 20%	500 ml	400 ml	300 ml	200 ml
Total energy content	2300 kcal	1900 kcal	1400 kcal	900 kcal

The content of the three chambers have to be mixed before use, by opening of the peelable seals.

1000 ml of the mixture contain:

Purified soybean oil	39 g
Glucose (anhydrous)	97 g
Alanine	4.7 g
Arginine	3.3 g
Aspartic acid	0.99 g
Phenylalanine	2.3 g
Glutamic acid	1.6 g
Glycine	2.3 g
Histidine	2.0 g
Isoleucine	1,6 g
Leucine	2.3 g
Lysine	2.6 g
Methionine	1.6 g
Proline	2.0 g
Serine	1.3 g
Threonine	1.6 g
Tryptophan	0.56 g
Tyrosine	0.07 g
Valine	2.1 g
Sodium glycerophosphate (anhydrous)	1.5 g
Calcium chloride	0.22 g
Potassium chloride	1.7 g
Magnesium sulphate	0.47 g
Sodium acetate	1.4 g
• Amino acide	33 g
• Nitrogen	5,3 g
• Fat	39 g
• Carbohydrates	
- Glucose (dextrose)	97 g
• Energy content	
- total	910 kcal
- Non protein	780 kcal
• Electrolytes	
- Sodium	31 mmol
- Potassium	23 mmol
- Magnesium	4 mmol
- Calcium	2 mmol
- Phosphate	9.7 mmol
- Sulphate	4 mmol
- Chloride	45 mmol
- Acetate	38 mmol
• Osmolality	approx. 1230 mosm/kg water
• Osmolarity	approx. 1060 mosmol/litre
• pH	approx. 5.6

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

Dosage and administration
The dose should be individualised and the choice of bag size should be made with regard to the patients clinical condition, body weight and nutritional requirements. To provide total parenteral nutrition, trace elements and vitamins should be given additionally.

Adult patients
The nitrogen requirements for maintenance of body protein mass depend on the patients 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. This corresponds 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.

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 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. Kabiven is recommended to be infused 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 active substances or excipients.
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 under 2 years of age

Special warnings and special 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, such as in 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 potassium intake 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.

Undesirable effects
See above "Fat overload syndrome".

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 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 patients clinical condition, such as renal function impairment or infection.

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

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

Overdose
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 haemodiafiltration may be necessary.

Pharmaceutical precautions

- Kabiven should only be mixed and used if the solutions are clear and colourless or slightly yellow and if the emulsion is white and homogeneous.
- Do not store above 25°C. Store in overpouch. Do not freeze. It is recommended to store the bag in the outer carton. Do not use if package is damaged.
- The contents of the three separate chambers have to be mixed before use. 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.
- Only medicinal or nutritional solutions for which compatibility has been documented may be added to Kabiven. Additions should be made aseptically. 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. 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.

Manufactured by:
Fresenius Kabi AB, S-751 74 Uppsala, Sweden

and

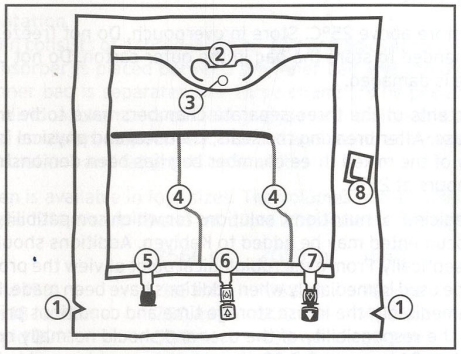
Fresenius Kabi Austria GmbH, A-8055 Graz, Austria

Packsizes:
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

April 2019

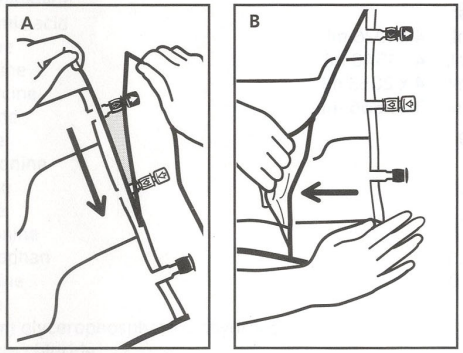
Kabiven Instructions for use

The bag



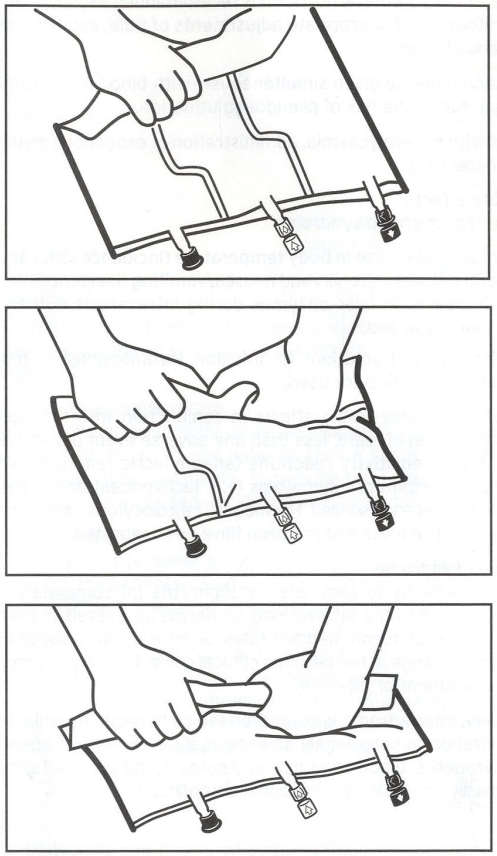
① Notches in the overpouch
② Handle
③ Hole for hanging the bag
④ Peelable seals
⑤ Blind port (only used during Manufacturing)
⑥ Additive port
⑦ Infusion port
⑧ Oxygen absorber

1. Removal of overpouch



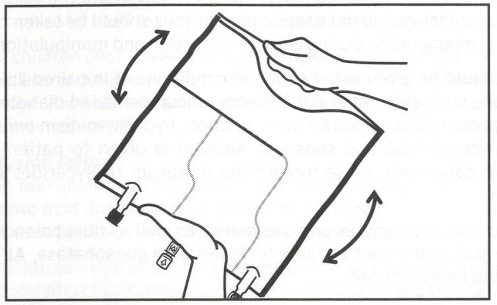
- To remove overpouch, hold the bag horizontally and tear from the notch close to the ports along the upper edge (A).
- Then simply tear the long side, pull off the overpouch and discard it along with the oxygen absorber (B).

2. Mixing



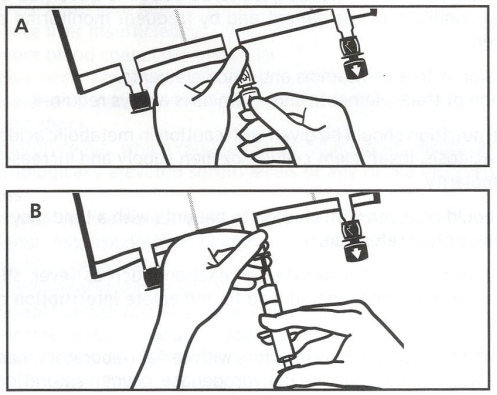
- Place the bag on a flat surface.
- Roll up the bag tightly from the handle side towards the ports, firstly with the right hand and then applying a constant pressure with the left hand until the vertical seals are broken. The vertical peel seals open due to the pressure of the fluid. The peel seals can also be opened before removing the overpouch.

Please note: The liquids mix easily although the horizontal seal remains closed.



- Mix the contents of the three chambers by inverting the bag three times until the components are thoroughly mixed.

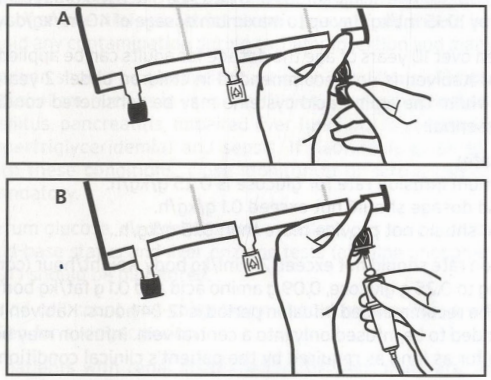
3. Finalising the preparation:



- Place the bag on a flat surface again. Shortly before injecting the additives, break off the tamper-evident arrow flag from the white additive port (A).

Please note: The membrane in the additive port is sterile.

- Hold the base of the additive port. Insert the needle, inject the additives (with known compatibility) through the centre of the injection site (B).
- Mix thoroughly between each addition by inverting the bag three times. Use syringes with needles of 18-23 gauge and a length of max. 40 mm.



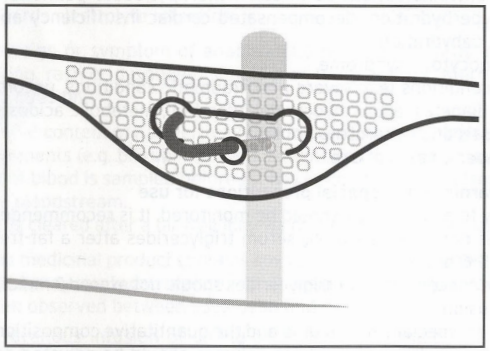
- Shortly before inserting the infusion set, break off the tamper evident arrow flag from the blue infusion port (A).

Please note: The membrane in the infusion port is sterile.

- Use a non-vented infusion set or close the air-inlet on a vented set.
- Hold the base of the infusion port.
- Push the spike through the infusion port.
  The spike should be fully inserted to secure it in place.

Please note: The inner part of the infusion port is sterile.

4. Hanging up the bag



- Hang the bag up by the hole below the handle.

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