Kabiven™ Perifer

Emulsion for infusion

FRESENIUS KABI

Presentation

Kabiven Perifer 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.

Kabiven Perifer is available in three sizes. The volumes of the components (Glucose 11%, Vamin 18 and Intralipid 20%) are the following:

	2400 ml	1920 ml	1440 ml
Glucose 11%	1475 ml	1180 ml	885 ml
Vamin 18 Novum	500 ml	400 ml	300 ml
Intralipid 20%	425 ml	340 ml	255 ml
Total energy content	1700 kcal	1400 kcal	1000 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	35 g
Glucose (anhydrous)	68 g
Alanine	3.3 g
Arginine	2.4 g
Aspartic acid	0.71 g
Phenylalanine	1.6 g
Glutamic acid	1.2 g
Glycine	1.6 g
Histidine	1.4 g
Isoleucine	1.2 g
Leucine	1.6 g
Lysine	1.9 g
Methionine	1.2 g
Proline	1.4 g
Serine	0.94 g
Threonine	1.2 g
Tryptophan	0.40 g
Tyrosine	0.05 g
Valine	1.5 g
Sodium glycerophosphate (anhydrous)	1.0 g
Calcium chloride	0.15 g
Potassium chloride	1.2 g
Magnesium sulphate	0.33 g
Sodium acetate	1.0 g
• Amino acids	24 g
• Nitrogen	3.8 g
• Fat	35 g
• Carbohydrates	
- Glucose (dextrose)	68 g

• Energy content	
- total	720 kcal
- Non protein	620 kcal
• Electrolytes	
- Sodium	22 mmol
- Potassium	17 mmol
- Magnesium	2.8 mmol
- Calcium	1.4 mmol
- Phosphate	7.5 mmol
- Sulphate	2.8 mmol
- Chloride	32 mmol
- Acetate	27 mmol
• Osmolality	approx. 830 mosm/kg water
• Osmolarity	approx. 750 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 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 Perifer 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 weight/day) and a total energy of 20-30 kcal body weight/day corresponds to approx. 27-40 ml Kabiven Perifer/kg b.w./day.

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. 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 Perifer 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 Perifer is 12-24 hours.

Method and duration of administration

Intravenous infusion into a Perifer 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, daily rotation of infusion site is recommended.

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 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 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 Perifer should be given with caution in conditions of impaired lipid metabolism due to renal insufficiency, uncompensated diabetes mellitus, pancreatitis, impaired liver function, hypothyroidism (with hypertriglyceridaemia) or sepsis. If Kabiven Perifer 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 Perifer 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 Perifer 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 Perifer 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.

Perifer infusion
As with all hypertonic solutions, thrombophlebitis may occur if Perifer 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.

Undesirable effects
The infusion 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.

Reports of other undesirable effects in conjunction with the included components are extremely rare. Hypersensitivity reactions (anaphylactic reaction, skin rash, urticaria), respiratory symptoms (e.g. tachypnoea) and hyper/hypotension have been described. Haemolysis, reticulocytosis, abdominal pain, headache, nausea, vomiting, 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 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.

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. An impaired capacity to eliminate fat 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. These changes are invariably reversible on discontinuation of the fat infusion

If symptoms of overdose occur, the infusion should be slowed down or discontinued.

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

Pharmaceutical precautions

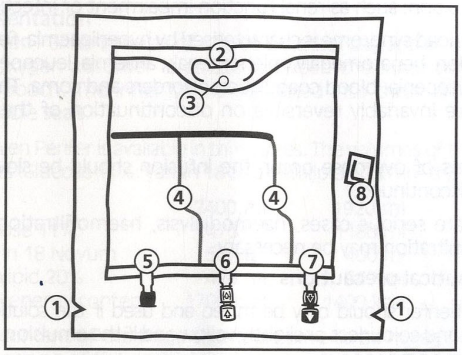
- Kabiven Perifer should only be mixed and used if the solutions are clear and colourless or slightly yellow and if the emulsion is white and homogenous.
- Store in overpouch, not above 25 °C. Do not freeze. It is recommended to store the bag in the outer carton. Do not use if package is damaged.
- The 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 Perifer. Additions should be made aspetically. 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. However if 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.

Packsize:
1 x 1440 ml, 4 x 1440 ml
1 x 1920 ml, 2 x 1920 ml (Excel), 4 x 1920 ml (Biofine)
1 x 2400 ml, 2 x 2400 ml (Excel), 3 x 2400 ml (Biofine)

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

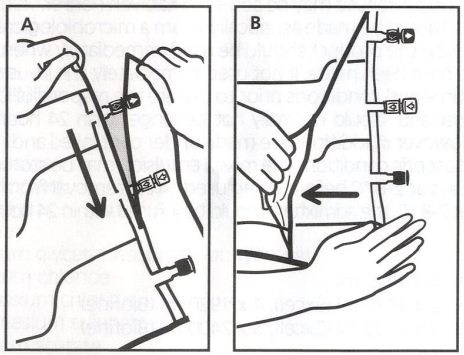
Kabiven™ Perifer Instructions for use

The bag



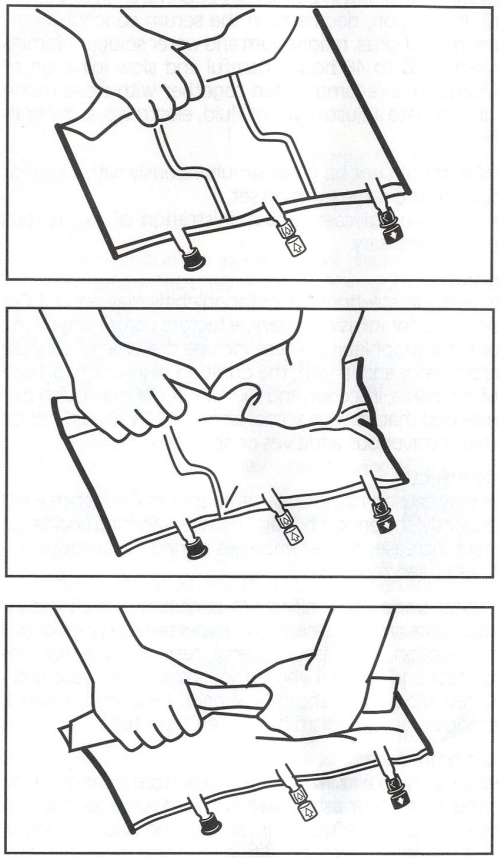
① Notches in the overpouch
② Handle
③ Hole for hanging the bag
④ Peelable seals
⑤ Blind port (only used during Manufacturing)
⑥ Additive port
⑦ Infusion port
⑧ Oxygen absorber

1. Removal of overpouch



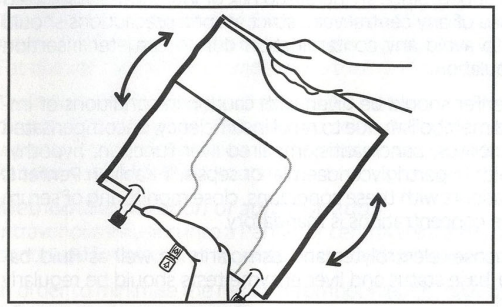
- To remove overpouch, hold the bag horizontally and tear from the notch close to the ports along the upper edge (A).
- Then simply tear the long side, pull off the overpouch and discard it along with the oxygen absorber (B).

2. Mixing



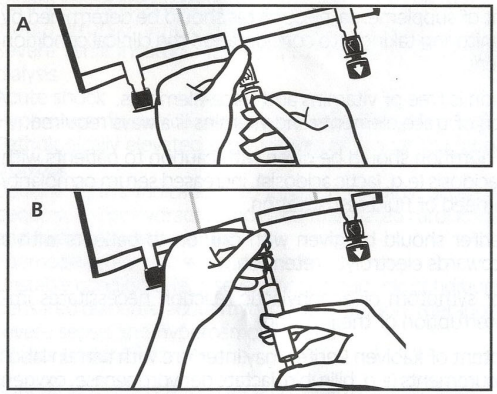
- Place the bag on a flat surface.
- Roll up the bag tightly from the handle side towards the ports, firstly with the right hand and then applying a constant pressure with the left hand until the vertical seals are broken. The vertical peel seals open due to the pressure of the fluid. The peel seals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

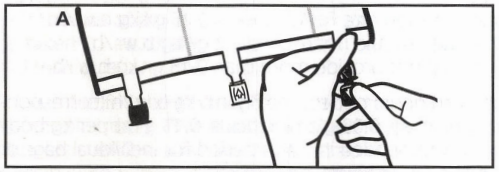
3. Finalising the preparation:

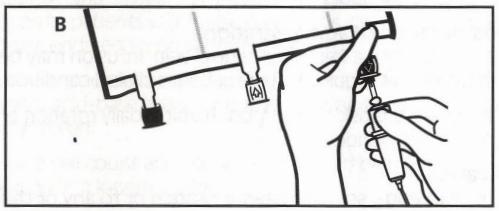


- Place the bag on a flat surface again. Shortly before injecting the additives, break off the tamper-evident arrow flag from the white additive port (A).

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.





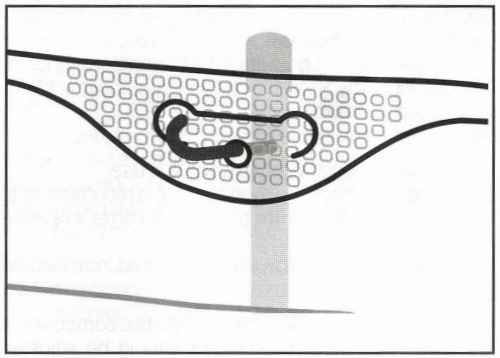
- Shortly before inserting the infusion set, break off the tamper evident arrow flag from the blue infusion port (A).

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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