

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Vaminoven 18 solution for infusion.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

	<u>1000 ml</u>	<u>750 ml</u>	<u>500 ml</u>
Alanine	16.00 g	12.0 g	8.00 g
Arginine	11.30 g	8.48 g	5.65 g
Aspartic acid	3.40 g	2.55 g	1.70 g
Glutamic acid	5.60 g	4.20 g	2.80 g
Glycine	7.90 g	5.93 g	3.95 g
Histidine	6.80 g	5.10 g	3.40 g
Isoleucine	5.60 g	4.20 g	2.80 g
Leucine	7.90 g	5.93 g	3.95 g
Lysine hydrochloride	11.30 g	8.48 g	5.65 g
corresponding to Lysine	9.00 g	6.75 g	4.5 g
Methionine	5.60 g	4.20 g	2.80 g
Phenylalanine	7.90 g	5.93 g	3.95 g
Proline	6.80 g	5.10 g	3.40 g
Serine	4.50 g	3.38 g	2.25 g
Threonine	5.60 g	4.20 g	2.80 g
Tryptophan	1.90 g	1.43 g	0.45 g
Tyrosine	0.23 g	0.17 g	0.12 g
Valine	7.30 g	5.48 g	3.65 g
Sodium acetate	8.17 g	6.13 g	4.08 g
<i>corresponding to:</i>			
Sodium acetate anhydrous	4.95 g	3.69 g	2.46 g
Potassium chloride	5.97 g	4.48 g	2.98 g
Calcium chloride	0.98 g	0.74 g	0.49 g
<i>corresponding to:</i>			
Calcium chloride anhydrous	0.74 g	0.56 g	0.37 g
Magnesium sulphate heptahydrate	3.29 g	2.47 g	1.65 g
<i>corresponding to:</i>			
Magnesium sulphate anhydrous	1.60 g	1.20 g	0.80 g
Sodium glycerophosphate (anhydrous)	5.04 g	3.78 g	2.52 g
Corresponding to:			
Na ⁺	107.00 mmol	80.20 mmol	53.50 mmol
K ⁺	80.00 mmol	60.00 mmol	40.00 mmol
Ca ²⁺	6.70 mmol	5.03 mmol	3.35 mmol
Mg ²⁺	13.40 mmol	10.00 mmol	6.70 mmol
Cl ⁻	155.00 mmol	116.00 mmol	77.50 mmol
P	23.30 mmol	17.40 mmol	11.60 mmol
Acetate	126.00 mmol	94.50 mmol	63.00 mmol
Sulphate	13.30 mmol	9.98 mmol	6.65 mmol
Total amino acids	113.00 g	84.8 g	56.50 g

Total nitrogen	18.00 g	13.5 g	9.00 g
Energy content	1900.00 kJ	1425.0 kJ	950.00 kJ
or	450.00 kcal	or 338.00 kcal	or 225.00 kcal
Osmolarity theoretical	1455 mosm/l		
Osmolality theoretical	1590 mosm/kg H ₂ O		
Titration acidity up to pH 7.4	approx. 72 mmol/l		
pH value	5.4-5.8		
Density	1.048 g/ml		

For excipients see 6.1.

3 PHARMACEUTICAL FORM

Solution for infusion.

The solution is clear and colourless to slightly yellow.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Supply of essential and non-essential amino acids and electrolytes as a part of parenteral nutrition for patients when oral or enteral nutrition is impossible, insufficient or contraindicated.

4.2 Posology and method of administration

The amino acid/nitrogen requirements for maintenance of body protein mass depend on the patient's condition (e.g. nutritional state and degree of catabolic stress).

Adults and Elderly patients

The requirements are 0.1-0.15 g nitrogen (= 0.6-1.0 g amino acids)/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 0.15-0.3 g nitrogen (= 1.0-2.0 g amino acids)/kg body weight/day.

The dose range 0.1-0.3 g nitrogen (= 0.6-2.0 g amino acids)/kg body weight/day corresponds to 6-17 ml Vaminoven 18/kg body weight/day and to 400-1200ml/70kg patient/day.

In obese patients the dose should be based on the estimated ideal weight.

Maximum daily dose

17 ml Vaminoven 18/kg body weight/day (= 2.0 g amino acids/kg body weight/day).

Maximum infusion rate

Vaminoven 18 should be infused slowly, at a rate not exceeding 0.9 ml/kg body weight/hour (= 0.1 g amino acids/kg body weight/hour).

Children

The composition of Vaminoven 18 is not suitable for the use in new-borns or infants under 2 years of age. The growing child needs in general a higher nitrogen dose than adults and elderly.

The doses for children recommended below should be achieved by a subsequent increase over 2-3 days from a starting dose of 0.15 g nitrogen (= 1.0 g amino acids/kg body weight/day).

For patients with a body weight of 10-30 kg, a dose of 0.3 g nitrogen (2.0 g amino acids)/kg body weight/day is generally recommended. For a body weight above 30 kg, a dose of 0.25 g nitrogen (= 1.5 g amino acids/kg body weight/day) is recommended but might be increased in severe metabolic stress.

Method and duration of administration

Intravenous use, infusion into a central vein.

After mixing with other nutrients, depending on the osmolarity of the admixture, infusion into a peripheral vein may be considered. Daily rotation of the infusion site minimises the risk of thrombophlebitis.

Infusion may be continued for as long as required by the patient's clinical condition.

Adequate energy supply must be provided for parenterally administered amino acids to be retained by the body and used for protein synthesis. Sources of intravenous calories include glucose solutions and fat emulsions (a source of calories and essential fatty acids) and these should be administered concurrently.

For complete nutritional support, and particularly if receiving prolonged intravenous feeding, total parenteral nutrition (TPN) regimens must also include vitamins and trace elements, as necessary. Additional electrolytes may also be necessary.

4.3 Contraindications

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4.4 Special warnings and precautions for 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.

Serum electrolytes and osmolarity as well as fluid balance, acid-base status, blood glucose, renal function and liver enzyme tests (alkaline phosphatase, ALT, AST) should be monitored regularly. Vaminoven 18 should be used with caution in patients with a tendency towards electrolyte retention.

In patients with renal insufficiency, the phosphate and potassium intake should be carefully controlled to prevent hyperphosphataemia and hyperkalaemia. These patients require particularly careful monitoring of electrolyte requirements.

Parenteral nutrition should be given with caution in metabolic acidosis and increased serum osmolarity.

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.

The appearance of any sign or symptom of an anaphylactic reaction (such as fever, shivering, rash, swelling or dyspnoea) necessitates the immediate interruption of the infusion.

Intravenous infusion of amino acids may be accompanied by increased urinary excretion of the essential trace elements, particularly 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. A fall in serum concentrations of potassium, phosphorous, 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.

Amino acid solutions may precipitate acute folate deficiency, therefore folic acid should be given daily.

Care should be exercised in the administration of large volume infusion fluids to patients with cardiac insufficiency.

Infusions of amino acids must be administered with caution to patients with disturbances in protein metabolism.

As with all hypertonic solutions, thrombophlebitis may occur if peripheral veins are used for infusions. Daily inspections of the insertion area and rotation of the infusion site are recommended. It is advised that venous access sites for parenteral nutrition should not be used for other intravenous additives or solutions.

The choice of a peripheral or central vein depends on the final osmolarity of the solution.

4.5 Interaction with other medicinal products and other forms of interaction

No interactions are known to date.

4.6 Pregnancy and lactation

No data are available for Vaminoven 18.

No specific studies have been performed to assess the safety of Vaminoven 18 solution for infusion in pregnancy or lactation. However clinical experience with similar parenteral amino acid solutions has shown no evidence of risk during pregnancy or breast-feeding. The risk/benefit relationship should be considered before administration of Vaminoven 18 solution for infusion to pregnant or breast-feeding women.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

	<i>Common</i> >1/100, <1/10	<i>Uncommon</i> >1/1000, <1/100	<i>Rare</i> >1/10000, <1/1000	<i>Very rare</i> <1/10000
<i>Metabolism and nutrition disorders</i>				Transient increases in liver enzymes
<i>Gastrointestinal disorders</i>		Nausea, vomiting		
<i>General disorders and administration site conditions</i>	Trombophlebitis (if peripheral veins are used)			Allergic reaction

4.9 Overdose

Nausea, vomiting shivering, flushing and sweating and increased renal amino acid losses can occur, when amino acid solutions are infused at rates exceeding the recommended maximal rate or when overdosed.

If Vaminoven 18 is infused greatly in excess of recommended rates electrolyte abnormalities may occur. Overdosage of amino acids may lead to metabolic acidosis or hyperazotemia, specially in chronic renal failure patients.

If symptoms of overdose occur the infusion should be stopped immediately. The patient should be assessed with particular attention paid to the respiratory and cardiovascular systems. Biochemical monitoring should be carried out and the patient treated appropriately. Subsequently it may be possible to continue the infusion at a reduced dose.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Solutions for parenteral nutrition.

ATC Code: B05BA01

Pharmacological effects, other than nutritive ones, are not to be expected from amino acid solutions as long as they are infused according to the recommended dosage for parenteral nutrition.

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 thermogenic effect of amino acid infusion due to small increase in metabolic rate.

The electrolytes have no pharmacodynamic effects apart from contributing to normal electrolyte homeostasis.

5.2 Pharmacokinetic properties

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.

5.3 Preclinical safety data

Preclinical safety studies with Vaminoven 18 have not been performed. However, preclinical safety studies with amino acid and electrolyte solutions of various compositions and concentrations demonstrate good tolerance.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Acetic acid, glacial (pH-adjustment)

Water for injections

6.2 Incompatibilities

The solution contains calcium-ions. Addition of inorganic phosphate or hydrogen carbonate/carbonate may lead to precipitation.

Vaminoven 18 may only be mixed with other medicinal products for which compatibility has been documented. (*see section 6.4, Special precautions for storage and 6.6, Instructions for use and handling and disposal*).

6.3 Shelf Life

2 years in the overpouch.

After first opening the container.

Vaminoven 18 should be used immediately.

6.4 Special precautions for storage

Store in overpouch. Do not freeze.

After mixing with other medicinal products:

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 to 8°C, unless dilution has taken place in controlled and validated aseptic conditions. If storage can not be avoided and provided that the mixture is prepared under controlled and validated aseptic conditions the mixture may be stored up to 6 days at 2 to 8°C before being used. After removal from storage at 2 to 8°C, the admixture should be infused within 24 hours. (*see section 6.6, Instructions for use and handling and disposal*).

6.5 Nature and contents of container

The container consists of an inner bag and an overpouch. An oxygen absorber is placed between inner bag and overpouch.

- The inner bag consists of a poly(propylene/ethylene) copolymer, a thermoplastic elastomer and a copolyester.
- The overpouch consists of polypropylene, polyethylene terephthalate and poly (ethyl vinyl) alcohol
- The oxygen absorber consists of iron powder in a polymer sachet.

Bag sizes: 500 ml, 750 ml, 1000 ml

Pack sizes:

1 x 500 ml, 12 x 500 ml

1 x 750 ml, 8 x 750 ml

1 x 1000 ml, 6 x 1000 ml

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

Do not use if package is damaged.

Use only clear and colourless or slightly yellow solutions in undamaged containers.

For single use only. Any unused solution remaining after infusion should be discarded.

Compatibility

Vaminoven 18 may be aseptically admixed with other medicinal products such as fat emulsions, carbohydrates and electrolytes for which compatibility has been documented.

Compatibility data are available upon request.

7 MARKETING AUTHORISATION HOLDER

Fresenius Kabi Ltd
Cestrian Court
Eastgate Way
Runcorn, WA7 1NT
Cheshire
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA 0566/028/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 04 November 2003

Date of last renewal: 07 September 2006

10 DATE OF REVISION OF THE TEXT

February 2008