Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Aminoven 3.5% Glucose/Electrolytes solution for infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1000 ml solution for infusion contains:

Tyrosine	0.14 g
Isoleucine	1.75 g
Leucine	2.59 g
Lysine hydrochloride (= 2.31 g Lysine)	2.885 g
Methionine	1.505 g
Phenylalanine	1.785 g
Threonine	1.54 g
Tryptophan	0.70 g
Valine	2.17 g
Arginine	4.20 g
Histidine	1.05 g
Alanine	4.90 g
Glycine	3.85 g
Proline	3.92 g
Serine	2.275 g
Taurine	0.35 g
Glucose monohydrate (= 50 g Glucose anhydrous)	55.0 g
Sodium chloride	1.169 g
Calcium chloride dihydrate (= 0.222 g calcium chloride, anhydrous)	0.294 g
Magnesium chloride hexahydrate (= 0.286 g magnesium chloride, anhydrous)	0.61 g
Zinc chloride	0.00545 g
Sodium glycerophosphate, hydrated (= 3.241 g sodium glycerophosphate, anhydrous)	4.592 g
Potassium hydroxide (= 1.68 g potassium hydroxide, anhydrous)	1.98 g
Electrolytes:	
Na+	50 mmol/l
K+	30 mmol/l
Ca++	2 mmol/l
Mg++	3 mmol/l
Zn++	0.04 mmol/l
Cl-	46.7 mmol/l
Glycerophosphate--	15 mmol/l

Total amino acids:	35 g/l
Total nitrogen:	5.75 g/l
Total glucose:	50 g/l
Total energy:	1428 kJ/l (= 340 kcal/l)
Non-protein energy:	840 kJ/l (= 200 kcal/l)
Titratable acidity:	33.7 mmol NaOH/l

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Solution for infusion
The solution is clear and colourless to slightly yellow.
pH: 4.5 - 5.5
Theoretical osmolarity: 768.54 mosm/l.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Aminoven 3.5% Glucose/Electrolytes is indicated whenever parenteral supply of amino acids, electrolytes and glucose is needed for adult patients when oral or enteral nutrition is impossible, insufficient or contraindicated.

4.2 Posology and method of administration

For continuous peripheral intravenous application.
The daily dosage depends on the individual fluid needs of the patient.

Maximum daily dose:
40 ml Aminoven 3.5% Glucose/Electrolytes per kg body weight (equivalent to 1.4 g amino acids per kg body weight and 2.0 g glucose per kg body weight).

Maximum infusion rate:
1.7 ml Aminoven 3.5% Glucose/Electrolytes per kg body weight per hour (equivalent to 0.06 g amino acids per kg body weight and hour and 0.085 g glucose per kg body weight and hour).

If given as the sole source of nutrition Aminoven 3.5% Glucose/Electrolytes can be used for a maximum of one week in patients with a satisfactory to good nutritional condition and with mild to moderate catabolism.

4.3 Contraindications

Aminoven 3.5% Glucose/Electrolytes is contra-indicated in the following conditions:
Shock, hypoxia, hyponatraemia, hyperkalaemia, disturbances in amino acid metabolism, renal insufficiency, advanced liver insufficiency and insulin-refractory hyperglycaemia if the administration of more than 6 units of insulin per hour is required. Newborns, infants and children less than 12 years or less than 40 kg body weight.

General contra-indications to infusion therapy:
Acute pulmonary edema.
Hyperhydration.
Decompensated heart failure.
Hypotonic dehydration.
Unstable conditions (e.g. severe post-traumatic conditions, uncompensated diabetes, acute myocardial infarction, metabolic acidosis, severe sepsis and hyperosmolar coma).

4.4 Special warnings and precautions for use

Serum electrolytes, fluid balance, renal function and blood glucose levels must be controlled regularly.

Generally, infusion via peripheral veins can cause irritation of the vein intima and thrombophlebitis. To minimise the risk of vein irritation, daily controls of the puncture site are recommended.

The choice of a peripheral or central vein depends on the final osmolarity of the mixture. The general accepted upper limit for peripheral infusion is 800 mosm/l, but it varies considerably with the age and the general condition of the patient and the venosity of the peripheral veins.

Lipids, vitamins, additional electrolytes and trace elements should be administered as required.

In cases of hypokalemia and/or hyponatremia adequate amounts of potassium and/or sodium should be supplied simultaneously.

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

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

4.5 Interaction with other medicinal products and other forms of interaction

No interactions are known to date.

Please also refer to section 6.2 ”Incompatibilities”.

4.6 Fertility, pregnancy and lactation

No specific studies have been performed to assess the safety of Aminoven 3.5% Glucose/Electrolytes in fertility, pregnancy and lactation. However, clinical experiences with similar parenteral amino acid solutions have shown no evidence of risk during pregnancy and breastfeeding. The risk/benefit relationship should be considered before administering Aminoven 3.5% Glucose/Electrolytes during pregnancy and breastfeeding.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

As with all infusions in peripheral veins injection site irritation and thrombophlebitis have been observed. Allergic reaction against any of the ingredients in Aminoven 3.5% Glucose/Electrolytes may occur.

Immune system disorders	*Frequency: not known (cannot be estimated from the available data :* Allergic reaction.
General disorders and administration site conditions	*Frequency: not known (cannot be estimated from the available data):* Injection site irritation. Thrombophlebitis.

The incidence of injection site irritation and thrombophlebitis may increase when Aminoven 3.5% Glucose/Electrolyte is administered peripherally over a longer period.
The risk of thrombophlebitis will also increase with increased osmolarity of the infused solution. The osmolarity of Aminoven 3.5% GE is 769 mosm/l.
Reactions that occur during overdose (see section 4.9 overdose) are usually reversible and regress when therapy is

discontinued.

Reporting 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 scheme listed below.

Ireland
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

As with other amino acid solutions shivering, vomiting, nausea, and increased renal amino acid losses can occur when Aminoven 3.5% Glucose/Electrolytes is given in overdose or the infusion rate is exceeded.
When Aminoven 3.5% Glucose/Electrolytes is given in overdose fluid overload, hyperglycaemia and electrolyte disturbances may occur.
Infusion should be stopped immediately in this case. It may be possible to continue with a reduced dosage.

There is no specific antidote for overdose. Infusion should be stopped immediately in such cases. Emergency procedures should be general supportive measures, with particular attention to respiratory and cardiovascular systems. Close biochemical monitoring would be essential and specific abnormalities treated appropriately.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Amino acids - solution for parenteral nutrition,
ATC code: B05BA01

The amino acids contained in Aminoven 3.5% Glucose/Electrolytes are all naturally occurring physiological compounds. As with the amino acids derived from the ingestion and assimilation of food proteins, parenterally-administered amino acids enter the body pool of free amino acids and all subsequent metabolic pathways.

Glucose is metabolised as an energy carrier by almost all tissues. It enters the glycolysis after phosphorylation. The metabolism of glucose as an energy substrate or as precursor for endogenous syntheses is well known.

The electrolytes contained in Aminoven 3.5% Glucose/Electrolytes are indispensable nutrients for the maintenance and correction of fluid and electrolyte homeostasis.
The trace element zinc has different physiological functions in the organism.

5.2 Pharmacokinetic properties

The amino acids in Aminoven 3.5% Glucose/Electrolytes enter the plasma pool of the corresponding free amino acids. From the intravascular space, amino acids distribute to the interstitial fluid and, individually regulated for each single amino acid, into the intracellular space of different tissues as required.
Plasma and intracellular free amino acid concentrations are endogenously regulated within narrow ranges, depending on the age, nutritional status and metabolic condition of the patient.
Balanced amino acid solutions such as Aminoven 3.5% Glucose/Electrolytes do not significantly alter the physiological

amino acid pool when infused at a constant and slow speed.

Characteristic changes in the physiological amino acid pool of the plasma are only foreseeable when the regulative function of essential organs such as the liver and kidneys are seriously impaired. In such cases specially formulated amino acid solutions may be recommended for restoring homeostasis.

In healthy persons, blood glucose concentrations are maintained within normal limits by insulin which facilitates the passage of glucose through cell membranes and other homeostatic mechanisms. Patients requiring parenteral nutrition are often in a metabolic condition with limited glucose tolerance which can make the administration of insulin necessary.
The distribution of electrolytes is regulated via their intra- and extracellular concentrations of specific ions.

Only a small proportion of the infused amino acids is eliminated by the kidneys.
For the majority of amino acids plasma half-lives between 10 and 30 minutes have been measured.

The elimination of electrolytes depends on requirements as well as the metabolic condition and the renal function of the patient.

In healthy persons glucose is not eliminated by the kidneys at all. In certain pathological conditions glucose can be eliminated by the kidneys when the maximum tubular reabsorption capacity (180 mg/100 ml resp. 10 mmol/l) is exceeded.

5.3 Preclinical safety data

Preclinical toxicity data are available for single amino acids but are not relevant to mixtures of amino acids in solutions such as Aminoven 3.5% Glucose/Electrolytes. No preclinical toxicity studies with Aminoven 3.5% Glucose/Electrolytes have been carried out, but studies with comparable amino acid solutions have shown no toxic effect. No toxic effects of glucose for parenteral nutrition have ever been reported and are not to be expected, since glucose is a physiological substance and ubiquitous nutrient. The electrolytes contained in Aminoven 3.5% Glucose/Electrolytes are also physiological compounds, whose provision is required by the organism for homeostasis. Toxicity has not been reported and is not foreseen when the electrolytes are supplemented according to the requirements.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Acetylcysteine
Malic acid
Water for injections

6.2 Incompatibilities

Incompatibilities may occur through the addition of polyvalent cations, e.g. calcium, especially when combined with heparin. Inorganic phosphate should not be added, because of possible precipitation of calcium- und magnesium phosphate.

Due to the increased risk of microbiological contamination and incompatibilities, amino acid solutions should not be mixed with other drugs.

Should it become necessary to add other nutrients, see section 6.3 c), 6.4, 6.6.

6.3 Shelf life

a) *Shelf-life of the medicinal product as packaged for sale*

1 year

b) *Shelf-life after first opening of the container*
Aminoven 3.5% Glucose/Electrolytes should be used with sterile transfer equipment immediately after opening. Any unused solutions should be discarded.

c) *Shelf-life after mixing with other components*
In general, TPN admixtures may be stored for a maximum period of 24 hours at 2 to 8°C, unless a longer storage period has been proven. See Section 6.4.

6.4 Special precautions for storage

Do not store above 25°C.
Keep container in the outer carton.
Do not freeze.

Storage precautions after mixing with other components:
Aminoven 3.5% Glucose/Electrolytes may be aseptically admixed with other nutrients such as fat emulsions, carbohydrates and electrolytes. Chemical and physical stability data for a number of admixtures stored at 4°- 8° C for up to 7 days are available from the manufacturer upon request.

From a microbiological point of view, TPN admixtures compounded in uncontrolled or unvalidated conditions should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and should normally be no longer than 24 hours at 2 to 8°C, unless mixing has taken place in controlled and validated aseptic conditions.

6.5 Nature and contents of container

Glass bottles**,** 500 ml and 1000 ml.
Type II, colourless glass, rubber closure/aluminium cap and outer carton

Packs of: 10 x 500 ml glass bottles (sales package).
6 x 1000 ml glass bottles (sales package).
1 x 500 ml glass bottle (sample package).

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

To be used immediately after the bottle is opened. For single use only.

Do not use Aminoven 3.5% Glucose/Electrolytes after expiry date.

Use only clear, particle-free solutions and undamaged containers.

Discard unused solutions. Any admixture remaining after infusion must be discarded.

Due to the increased risk of microbiological contamination and incompatibilities, amino acid solutions should not be mixed with other drugs.

Should it become necessary to add other nutrients, like carbohydrates, lipid emulsions, electrolytes, vitamins or trace elements to Aminoven 3.5% Glucose/Electrolytes for complete parenteral nutrition, care should be given to aseptic techniques, thorough mixing and, in particular, to compatibility.

Compatibility data are available from the manufacturer for a number of mixtures.

7 MARKETING AUTHORISATION HOLDER

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

8 MARKETING AUTHORISATION NUMBER

PA 566/14/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 26 November 1999

Date of last renewal: 06 January 2009

10 DATE OF REVISION OF THE TEXT

February 2015