Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Aminoplasmal 5% E without Carbohydrates Solution for Infusion.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1000 ml of solution contains:

Isoleucine	2.55	g
Leucine	4.45	g
Lysine Hydrochloride *(equivalent to lysine 2.80g)*	3.50	g
Methionine	1.90	g
Phenylalanine	2.55	g
Threonine	2.05	g
Tryptophan	0.90	g
Valine	2.40	g
Arginine	4.60	g
Histidine	2.60	g
Glycine	3.95	g
Alanine	6.85	g
Proline	4.45	g
Aspartic Acid	0.65	g
Asparagine monohydrate *(equivalent to asparagine 1.64 g)*	1.86	g
Acetylcysteine *(equivalent to cysteine 0.25 g)*	0.34	g
Glutamic acid	2.30	g
Ornithine hydrochloride *(equivalent to ornithine 1.25 g)*	1.60	g
Serine	1.20	g
Tyrosine	0.30	g
Acetyltyrosine *(equivalent to tyrosine 0.35 g)*	0.43	g
Sodium acetate trihydrate	3.95	g
Potassium acetate	2.45	g
Magnesium acetate tetrahydrate	0.56	g
Sodium dihydrogen phosphate dihydrate	1.40	g
Sodium hydroxide	0.20	g
Malic acid	1.01	g

Electrolyte concentrations

Sodium	43	mmol/l
Potassium	25	mmol/l
Magnesium	2.6	mmol/l
Acetate	59	mmol/l
Chloride	29	mmol/l
Dihydrogen phosphate	9.0	mmol/l
L-Malate	7.5	mmol/l
Total amino acids content	50	g/l
Total nitrogen content	8.0	g/l

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Solution for infusion
A clear, colourless or faintly straw-coloured aqueous solution

Caloric value	835	kJ/l ≙ 200 kcal/l
Osmolarity	590	mOsm/l
Acidity (titration to pH 7.4),approx.	18	mmol/l
pH	5.0 – 7.5	

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Supply of amino acids as a substrate for protein synthesis in parenteral nutrition, when oral or enteral nutrition is impossible, insufficient or contraindicated.

In parenteral nutrition, amino acid infusions should always be combined with adequate calorie supply, e. g. in the form of carbohydrate solutions.

4.2 Posology and method of administration

The dosage is adjusted according to the individual need of amino acids, electrolytes and fluid, depending on the patient's clinical condition (nutritional status and/or degree of nitrogen catabolism due to underlying disease).

Adults and adolescents from 15 to 17 years:

Average daily dose
20 – 40 ml/kg body weight (BW) ≙ 1.0 – 2.0 g of amino acids/kg BW,
≙ 1400 – 2800 ml for a patient of 70 kg BW

Maximum daily dose:
40 ml/kg BW ≙ 2.0 g of amino acids/kg BW,
≙ 140 g of amino acids for a patient of 70 kg BW
≙ 2800 ml for a patient of 70 kg BW

Maximum infusion and drop rates, respectively:

2.0 ml/kg BW/h ≙ 0.1 g of amino acids/kg BW/h,
≙ 45 drops/min for a patient of 70 kg BW
≙ 2.34 ml/min for a 70 kg patient

Children and adolescents up to 14 years:

The dosages for this age group as stated below are average values for guidance. The exact dosage should be adjusted individually according to age, developmental stage and prevailing disease.

Daily doses for:

3rd to 5th year of life: 30 ml/kg BW, corresponding to 1.5 g amino acids/kg BW
6th to 14th year of life: 20 ml/kg BW, corresponding to 1.0 g amino acids/kg BW

Maximum infusion rate:
2 ml/kg BW/h, corresponding to 0.1 g amino acids/kg BW/h

In the case of amino acid requirements of 1 g/kg BW/day or more, particular attention should be paid to the limitations of fluid input. To avoid fluid overload, amino acid solutions with higher amino acid content may have to be used in such situations.

Method of administration and duration of use

Intravenous use

The solution can be administered as long as there is an indication for parenteral nutrition.

Aminoplasmal – 5 % E without Carbohydrates is only one component of parenteral nutrition. In parenteral nutrition, amino acid supply must be combined with supply of calorie sources, essential fatty acids, vitamins, and trace elements.

4.3 Contraindications

Contraindications related to the product or to parenteral nutrition

- Hypersensitivity to any of the ingredients present in the solution
- Congenital abnormalities of amino acid metabolism
- Severe circulatory disorders with vital risk, (e.g. shock)
- Hypoxia
- Metabolic acidosis
- Advanced liver disease
- Severe renal insufficiency without access to haemofiltration or haemodialysis
- High and pathological plasma concentration of one of the electrolytes contained in the product

This solution must not be administered to neonates, infants or children up to the completed 2nd year as the nutrient relations do not properly meet the special paediatric requirements.

Contraindications related to infusion therapy in general

- Uncompensated cardiac insufficiency
- Acute pulmonary oedema
- Hyperhydration

4.4 Special warnings and precautions for use

This solution should only be administered after careful benefit-risk assessment in the presence of disorders of amino acid metabolism of other origin than stated under *section 4.3, Contraindications*.

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

In patients with hepatic or renal insufficiency, the dose must be adjusted according to individual requirements.

Caution is to be exercised in patients with increased serum osmolarity

Electrolyte and fluid imbalances such as hypotonic dehydration and hyponatraemia, should be corrected by adequate supply of fluid and electrolytes prior to parenteral nutrition.

Serum electrolytes, blood glucose, fluid balance, acid-base balance and renal function (BUN, creatinine) should be monitored regularly.

Monitoring should also include serum protein and liver function tests.

Aminoplasmal – 5 % E without Carbohydrates is applicable as part of a total parenteral nutrition regimen in combination with adequate amounts of energy supplements (carbohydrate solutions, fat emulsions), vitamins and trace elements.

If the solutions are administered in combination with other nutrient solutions, the possibility of peripheral venous infusion depends on the osmolarity of the resulting mixture.

The site of infusion should be checked daily for signs of inflammation or infection.

4.5 Interaction with other medicinal products and other forms of interaction

Pharmacological interactions are not known.

4.6 Pregnancy and lactation

Studies in pregnant or breast-feeding women have not been conducted with this medicinal product. There are no pre-clinical data regarding the administration of Aminoplasmal – 5 % E without Carbohydrates during pregnancy.

Aminoplasmal – 5 % E without Carbohydrates should therefore be administered with caution during pregnancy and lactation and only if deemed clearly indicated after assessment of its benefits and possible risks.

4.7 Effects on ability to drive and use machines

This medicinal product has no effect on the ability to drive and to use machines.

4.8 Undesirable effects

Undesirable effects that, however, are not specifically related to the product but to parenteral nutrition in general may occur, especially at the beginning of parenteral nutrition.

Uncommon (< 1:100, ≥ 1:1000 of treated patients):

Gastrointestinal disorders:	nausea, vomiting
General disorders:	headache, shivering, fever

4.9 Overdose

Symptoms
Overdose or too high infusion rates may lead to intolerance reactions manifesting in the form of shivering, nausea, vomiting, and renal amino acid losses.

Treatment
If intolerance reactions occur, the amino acid infusion should be interrupted and resumed later at a lower infusion rate.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmaco-therapeutic group: Solutions for parenteral nutrition
ATC code: B05B A10

The aim of parenteral nutrition is the supply of all nutrients necessary for the growth, maintenance and regeneration of body tissues etc.

Amino acids are of special importance as they partly are essential for protein synthesis. Intravenously administered amino acids are incorporated in the respective intravascular and intracellular amino acid pools. Both endogenous and exogenous amino acids serve as substrate for the synthesis of functional and structural proteins.

To prevent the metabolisation of amino acids for energy production, and also to fuel the other energy consuming processes in the organism, simultaneous energy supply (in the form of carbohydrate or fat) is necessary.

5.2 Pharmacokinetic properties

Because Aminoplasmal – 5 % E without Carbohydrates is infused intravenously, the bio-availability of the amino acids and electrolytes contained in the solution is 100 per cent.

The composition of Aminoplasmal – 5 % E without Carbohydrates is based on the results of clinical investigations of the metabolism if intravenously administered amino acids.

The quantities of the amino acids contained in Aminoplasmal – 5 % E without Carbohydrates have been chosen so that a homogenous increase of the concentrations of all plasma amino acids is achieved. The physiological relations of plasma amino acids, i. e. the amino acid homeostasis is thus maintained during infusion of Aminoplasmal – 5 % E without Carbohydrates.

Amino acids that do not enter protein synthesis, are metabolized as follows. The amino group is separated from the carbon skeleton by transamination. The carbon chain is either oxidized directly to CO_2 or utilized as substrate for gluconeogenesis in the liver. The amino group is also metabolized in the liver to urea.

5.3 Preclinical safety data

Preclinical studies have not been performed with this medicinal product.

Aminoplasmal – 5 % E without Carbohydrates only contains amino acids and electrolytes that are substrates of human metabolism. Therefore, no toxic reactions are expected to occur as long as the indications contraindications and dosage recommendations are duly observed.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Disodium Edetate
Water for Injections

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in *section 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.*

6.3 Shelf Life

Unopened: 3 years

Shelf life after first opening the container

The medicinal product must be used immediately.

Shelf life after mixing with other components

Chemical and physical compatibility of any admixtures must be checked before administration.

From the microbiological point of view, mixtures should be administered immediately after preparation. If not administered immediately, storage times and conditions of mixtures prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 °C – 8 °C, unless mixing has taken place under controlled and validated aseptic conditions.

6.4 Special precautions for storage

Do not store above 25^{o}C

Keep bottles in the outer carton in order to protect from light.
Do not freeze

6.5 Nature and contents of container

Aminoplasmal – 5 % E without Carbohydrates is supplied in colourless glass bottles (glass type II Ph. Eur.) sealed with rubber stoppers.

Contents: 500 ml, available in packs of 10 bottles.

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

Containers are for single use only. Discard any unused contents remaining after the end of the infusion.

The solution should only be used if the closure of the container is not damaged and if the solution is clear.

Use a sterile giving set for administration.

If in the setting of complete parenteral nutrition it is necessary to add other nutrients such as carbohydrates, lipids, vitamins and trace elements to this medicinal product, admixing must be performed under strict aseptic conditions. Mix well after admixture of any additive. Pay special attention to compatibility.

7 MARKETING AUTHORISATION HOLDER

B. Braun Medical Limited
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8 MARKETING AUTHORISATION NUMBER

PA 0179/019/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

August 2007