

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Aminoplasmal B. Braun 10 % E

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

The solution for infusion contains:

	Per 1 mL		Per 250 mL		Per 500 mL		Per 1000 mL	
Isoleucine	5.00	mg	1.25	g	2.50	g	5.00	g
Leucine	8.90	mg	2.23	g	4.45	g	8.90	g
Lysine hydrochloride (\triangle Lysine)	8.56 (6.85)	mg (mg)	2.14 (1.71)	g (g)	4.28 (3.43)	g (g)	8.56 (6.85)	g (g)
Methionine	4.40	mg	1.10	g	2.20	g	4.40	g
Phenylalanine	4.70	mg	1.18	g	2.35	g	4.70	g
Threonine	4.20	mg	1.05	g	2.10	g	4.20	g
Tryptophan	1.60	mg	0.40	g	0.80	g	1.60	g
Valine	6.20	mg	1.55	g	3.10	g	6.20	g
Arginine	11.50	mg	2.88	g	5.75	g	11.50	g
Histidine	3.00	mg	0.75	g	1.50	g	3.00	g
Alanine	10.50	mg	2.63	g	5.25	g	10.50	g
Glycine	12.00	mg	3.00	g	6.00	g	12.00	g
Aspartic acid	5.60	mg	1.40	g	2.80	g	5.60	g
Glutamic acid	7.20	mg	1.80	g	3.60	g	7.20	g
Proline	5.50	mg	1.38	g	2.75	g	5.50	g
Serine	2.30	mg	0.58	g	1.15	g	2.30	g
Tyrosine	0.40	mg	0.10	g	0.20	g	0.40	g
Sodium acetate trihydrate	2.858	mg	0.715	g	1.429	g	2.858	g
Potassium acetate	2.453	mg	0.613	g	1.227	g	2.453	g
Sodium hydroxide	0.360	mg	0.090	g	0.180	g	0.360	g
Magnesium chloride hexahydrate	0.508	mg	0.127	g	0.254	g	0.508	g
Disodium phosphate dodecahydrate	3.581	mg	0.895	g	1.791	g	3.581	g

<i>Electrolyte concentrations:</i>	<i>mmol/l</i>
Sodium	50
Potassium	25
Magnesium	2.5
Acetate	46
Chloride	52
Phosphate	10
Citrate	1.0 - 2.0

Amino acid content	100 g/l
Nitrogen content	15.8 g/l

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for infusion

Clear, colourless or faintly straw-coloured solution, free from particles.

Energy [kJ/l (kcal/l)]	1675 (400)
Theoretical osmolarity [mOsm/]	1021
Acidity (titration to pH 7.4) [mmol NaOH/l]	approx. 26
pH	5.7 – 6.3

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Supply of amino acids and a limited amount of electrolytes for parenteral nutrition, when oral or enteral nutrition is impossible, insufficient or contraindicated. For adults, adolescents and children over 2 years of age.

4.2 Posology and method of administration

Posology

The dosage has to be adjusted according to the amino acids, electrolytes, and fluid requirements depending on the clinical condition of the patient (nutritional status and/or degree of nitrogen catabolism due to underlying disease).

Adults and adolescents from 14 to 17 years:

Daily dose:

1.0 – 2.0 g amino acids/kg body weight \triangleq 10-20 ml /kg body weight
 \triangleq 700–1400 ml for a 70 kg patient

Maximum infusion rate:

0.1 g amino acids/kg body weight/h \triangleq 1.0 ml/kg body weight/h
 \triangleq 1.17 ml/min for a 70 kg patient

Paediatric population

Newborn infants, infants and toddlers less than two years of age

Aminoplasmal B. Braun 10% E is contraindicated in newborn infants, infants and toddlers less than 2 years of age (see section 4.3).

Children and adolescents 2 to 13 years

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

Daily dose for children 2 to 4 years old:

1.5 g amino acids/kg body weight \triangleq 15 ml/kg body weight

Daily dose for children 5 to 13 years old:

1.0 g amino acids/kg body weight \triangleq 10 ml/kg body weight

Critically ill children:

For critically ill patients the advisable amino acid intake may be higher (up to 3.0 g amino acids/kg body weight per day).

Maximum infusion rate:

0.1 g amino acids/kg body weight/h \triangleq 1.0 ml/kg body weight/h

In the case of amino acid requirements of 1.0 g/kg body weight/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.

Patients with renal/hepatic impairment

The doses should be adjusted individually in patients with hepatic or renal insufficiency (see also section 4.4). Aminoplasmal B. Braun 10% E is contraindicated in severe hepatic insufficiency and severe renal insufficiency in absence of renal replacement therapy (see section 4.3).

Duration of use

This solution can be administered for as long as parenteral nutrition is indicated.

Method of administration

Intravenous use.

For central venous infusion only.

4.3 Contraindications

- Hypersensitivity to the active substances or to any of the excipients listed in section 6.1
- Congenital disturbances of amino acid metabolism
- Severe circulation disorders with vital risk (e.g. shock)
- Hypoxia
- Metabolic acidosis
- Severe hepatic insufficiency
- Severe renal insufficiency in absence of renal replacement therapy
- High and uncorrected plasma concentrations of one of the electrolytes contained in the product
- Decompensated cardiac insufficiency
- Acute pulmonary oedema
- Hyperhydration

The medicinal product must not be administered to newborn infants, infants and toddlers less than two years of age, because the amino acid composition does not properly meet the special requirements of this paediatric age group.

4.4 Special warnings and precautions for use

The medicinal product 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.

Caution should be exercised when infusing larger volumes of fluid in patients with cardiac insufficiency.

Caution should be exercised in patients with increased serum osmolarity.

Disturbances of fluid and electrolyte balance (e.g. hypotonic dehydration, hyponatraemia, hypokalaemia) should be corrected prior to parenteral nutrition.

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

Serum protein and hepatic function are to also be monitored.

Renal impairment

In patients with renal insufficiency, the dose must be carefully adjusted according to individual needs, the severity of organ insufficiency and the type of renal replacement therapy instituted (haemodialysis, haemofiltration etc.).

Hepatic impairment

In patients with hepatic insufficiency, the dose must be carefully adjusted according to individual needs and severity of organ insufficiency.

Amino acid solutions are only one component of parenteral nutrition. For complete parenteral nutrition, substrates for non-protein energy supply, essential fatty acids, electrolytes, vitamins, fluids and trace elements must be administered together with amino acids.

4.5 Interaction with other medicinal products and other forms of interaction

None known.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no data from the use of Aminoplasmal B. Braun 10% E in pregnant women. No animal reproductive studies have been performed with Aminoplasmal B. Braun 10% E. The use of Aminoplasmal B. Braun 10% E may be considered during pregnancy, if necessary. Aminoplasmal B. Braun 10% E should only be given to pregnant women after careful consideration.

Breast-feeding

Amino acids/metabolites are excreted in human milk, but at therapeutic doses of Aminoplasmal B. Braun 10% E, no effects on the breastfed newborns/infants are anticipated.

Nevertheless, breast-feeding is not recommended for mothers on parenteral nutrition.

Fertility

No data available.

4.7 Effects on ability to drive and use machines

Not relevant.

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.

Undesirable effects are listed according to their frequencies as follows:

Very common ($\geq 1/10$)

Common ($\geq 1/100$ to $< 1/10$)

Uncommon ($\geq 1/1,000$ to $< 1/100$)

Rare ($\geq 1/10,000$ to $< 1/1,000$)

Very rare ($< 1/10,000$)

Not known (cannot be estimated from the available data)

Immune system disorders

Not known: Allergic reactions

Gastrointestinal disorders

Uncommon: Nausea, vomiting

Reporting of 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. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form (<https://sideeffects.health.gov.il>).

4.9 Overdose

Symptoms of fluid and electrolytes overdose

Overdose or too-high infusion rates may lead to hyperhydration, electrolyte imbalance and pulmonary oedema.

Symptoms of amino acid overdose

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

Treatment

In such cases, the amino acid infusion must be interrupted and resumed later on at a lower infusion rate.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Blood substitutes and perfusion solutions, IV solutions, solutions for parenteral nutrition, combinations.

ATC code: B05BA10.

Mechanism of action

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 are partly 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.

Electrolytes administered with parenteral nutrition help to maintain the serum levels necessary for the physiological processes of the cell.

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

5.2 Pharmacokinetic properties

Absorption

Because this medicinal product is infused intravenously, the bioavailability of the amino acids contained in the solution is 100 %.

Distribution

Amino acids are incorporated in a variety of proteins in different tissues of the body. In addition, each amino acid is present as free amino acid in the blood and inside cells.

The composition of the amino acid solution is based upon the results of clinical investigations of the metabolism of intravenously administered amino acids. The quantities of the amino acids contained in the solution have been chosen so that a homogenous increase of the concentrations of all plasma amino acids is achieved. The physiological ratios of plasma amino acids, i. e.

amino acid homeostasis, are thus maintained during infusion of the medicinal product.

Normal foetal growth and development depend on a continuous supply of amino acids from the mother to the foetus. The placenta is responsible for the transfer of amino acids between the two circulations.

Biotransformation

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 CO₂ or utilized as substrate for gluconeogenesis in the liver. The amino group is also metabolized in the liver to urea.

Elimination

Only minor amounts of amino acids are excreted unchanged in the urine.

5.3 Preclinical safety data

No non-clinical studies have been performed with Aminoplasmal B. Braun 10% E. The amino acids and electrolytes contained in Aminoplasmal B. Braun 10% E are substances which occur naturally in the organism.

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

Acetylcysteine
Citric acid monohydrate (for pH-adjustment)
Water for injections

6.2 Incompatibilities

Aminoplasmal B. Braun 10% E may only be mixed with other nutrients such as carbohydrates, lipids, vitamins and trace elements for which compatibility has been documented.

Compatibility data for different additives (e.g. electrolytes, trace elements, vitamins) and the corresponding shelf life of such admixtures are available from the manufacturer on request. See also section 6.6.

6.3 Shelf life

Unopened

The expiry date of the product is indicated on the packaging materials

After first opening

The medicinal product should be used immediately after first opening.

After admixture of additives

Do not refrigerate.

From a microbiological point of view, unless the method of opening and mixing precludes the risk of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

6.4 Special precautions for storage

Do not store above 25 °C.

Keep the bottle in the outer carton in order to protect from light.

Do not freeze. Cool storage of the solution, below 15 °C, may lead to the formation of crystals that can, however, be easily and completely dissolved by gentle warming at 25 °C. Shake container gently to ensure homogeneity.

For storage conditions after mixing with additives, see section 6.3.

6.5 Nature and content of container

Bottles of colourless glass (type II), sealed with chlorobutyl-rubber stoppers.

Contents: 250 ml, available in packs of 10 bottles
500 ml, available in packs of 10 bottles
1000 ml, available in packs of 6 bottles

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements for disposal.

For single use only. Discard container and any unused contents after the infusion.

The solution should only be used if the closure of the container is not damaged and if the solution is clear, colourless or faintly straw-coloured solution, free from particles.

Use a sterile infusion set for administration.

If, in the setting of complete parenteral nutrition, it is necessary to add other nutrients such as carbohydrates, lipids, vitamins, electrolytes or 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 MANUFACTURER

B. Braun Melsungen AG
Carl-Braun-Straße 1,
D - 34212 Melsungen
Germany

8 REGISTRATION HOLDER

Lapidot Medical Import and Marketing Ltd.
8 Hashita st. Caesarea Industrial Zone 38900, Israel.

9 MARKETING AUTHORISATION NUMBER

150-94-33650-00

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