SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Aminoplasmal 15% Solution for Infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

The solution for infusion contains

	per 1 ml	per 500 ml	per 1000 ml
Isoleucine	5.850 mg	2.925 g	5.850 g
Leucine	11.40 mg	5.700 g	11.40 g
Lysine monohydrate	8.930 mg	4.465 g	8.930 g
(equivalent to lysine)	(7.950 mg)	(3.975 g)	(7.950 g)
Methionine	5.700 mg	2.850 g	5.700 g
Phenylalanine	5.700 mg	2.850 g	5.700 g
Threonine	5.400 mg	2.700 g	5.400 g
Tryptophan	2.100 mg	1.050 g	2.100 g
Valine	7.200 mg	3.600 g	7.200 g
Arginine	16.05 mg	8.025 g	16.05 g
Histidine	5.250 mg	2.625 g	5.250 g
Alanine	22.35 mg	11.175 g	22.35 g
Glycine	19.20 mg	9.600 g	19.20 g
Aspartic acid	7.950 mg	3.975 g	7.950 g
Glutamic acid	16.20 mg	8.100 g	16.20 g
Proline	7.350 mg	3.675 g	7.350 g
Serine	3.000 mg	1.500 g	3.000 g
Tyrosine	0.500 mg	0.250 g	0.500 g
Acetylcysteine	0.500 mg	0.250 g	0.500 g
(equivalent to cysteine)	(0.370 mg)	(0.185 g)	(0.370 g)

1000ml of *solution* contains:

Electrolyte concentrations		
Citrate	1.0 – 1.9	mmol/l
Sodium	5.3	mmol/l
Total amino acids	150	g/l
Total nitrogen	24.0	g/l

Excipient with known effect:

This medicinal product contains 5.3 mmol sodium per 1000 ml. To be taken into consideration in patients on a controlled sodium diet (see section 4.4).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for infusion
Clear, colourless up to faintly straw-coloured solution, practically free from visible particles.

Energy [kJ/l (kcal/l)]	2505 (600)
Theoretical osmolarity [mOsm/l]	1290
Acidity (titration to pH 7.4) [mmol NaOH/l]	approx.31
pH	5.7 - 6.3

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Supply of amino acids 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 individual need of amino acids and fluid, depending on the clinical condition of the patient (nutritional status and/or degree of nitrogen catabolism due to underlying disease).

Adults

Daily dose:

1.0 – 2.0 g amino acids/kg body weight	≙6.7 – 13.3 ml/kg body weight
	≙469 – 931 ml for a 70 kg patient

Maximum infusion rate:

0.1 g amino acids/kg body weight/h	≙0.67 ml/kg body weight/h
	≙0.78 ml/min for a 70 kg patient

Paediatric population
Newborn infants, infants and toddlers less than two years of age.

Aminoplasmal 15% is contraindicated in newborn infants, infants and toddlers less than 2 years of age (see section 4.3).

Children and adolescents 2 to 18 years
The dosages for the age groups 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 less than 3 years old:
1.0 - 2.5 g amino acids/kg body weight 6.64 - 16.6 ml/kg body weight

Daily dose for children 3 to 18 years old:
1.0 - 2.0 g amino acids/kg body weight 6.64 - 13.3 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 0.67 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). When given during dialysis amino acid losses into the dialysate have to be considered. Aminoplasmal 15% is contraindicated in severe hepatic insufficiency or decompensated liver cirrhosis with hepatic encephalopathy (grades III and IV) and severe renal insufficiency in absence of renal replacement therapy (see section 4.3).

Duration of use

This solution can be administered 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
- Inborn errors of amino acid metabolism
- Severe circulation disorders with vital risk (e.g. shock)
- Hypoxia
- Metabolic acidosis

- Severe hepatic insufficiency or decompensated liver cirrhosis with hepatic encephalopathy (grades III and IV)
- Severe renal insufficiency in absence of renal replacement therapy
- Decompensated cardiac insufficiency
- Acute pulmonary oedema
- Disturbances of the electrolyte and fluid balance

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.

Care should be exercised in the administration of large volume infusion fluids to 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 the administration of parenteral nutrition.

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

Monitoring should also include serum protein and liver function tests.

Renal impairment
In patients with renal insufficiency, the dose must be carefully adjusted according to individual needs, severity of organ insufficiency and the kind of instituted renal replacement therapy (haemodialysis, haemofiltration etc.). Amino acid losses due to the dialysis procedure had to be taken into consideration when adjusting the dose.

Hepatic impairment
In patients with hepatic insufficiency or decompensated liver cirrhosis with hepatic encephalopathy (grades I and II), 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.

This medicinal product contains approximately 122 mg sodium (5.3 mmol) per 1000 ml, corresponding to 6.1% of the WHO adult recommended maximum daily sodium intake of 2 g. This should be kept in mind when administering the product to patients requiring dietary restriction of sodium.

4.5 Interaction with other medicinal products and other forms of interaction

None known. For information on incompatibilities, see section 6.2.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no data from the use of Aminoplasmal 15% in pregnant women. No animal reproductive studies have been performed with Aminoplasmal 15%. The use of Aminoplasmal 15% may be considered during pregnancy, if necessary. Aminoplasmal 15% 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 15% no harmful effects on the breastfed newborn/infant 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 (≥ 1/10)
Common (≥ 1/100 to < 1/10)
Uncommon (≥ 1/1,000 to < 1/100)
Rare (≥ 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. Healthcare professionals are asked to report any suspected adverse reactions via Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Symptoms of fluid 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
If intolerance reactions occur, the amino acid infusion must be interrupted temporarily and resumed later on at a lower infusion rate.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Blood substitutes and perfusion solutions, i.v. solutions for parenteral nutrition, amino acids
ATC- code: B05B A01

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 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 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 bio-availability 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. the 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 metabolised as follows: The amino group is separated from the carbon skeleton by transamination. The carbon chain is either oxidised directly to CO2 or utilised as substrate for gluconeogenesis in the liver. The amino group is also metabolised 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 15%. The amino acids contained in Aminoplasmal 15% 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 fully observed.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium hydroxide

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

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products for which compatibility has not been documented. See section 6.6. Special care must be taken when using inorganic phosphate sources: Mixtures containing inorganic phosphate are incompatible with concentrations of amino acids less than 20 g/l and glucose less than 50 g/l and should be strictly avoided.

6.3 Shelf life

Unopened
3 years

After first opening
The medicinal product should be used immediately.

After admixture of additives
Chemical and physical in-use stability has been demonstrated for 7 days between 2 - 8 °C and additional 2 days at 20 - 25°C.

From a 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 30 °C.

Do not freeze.

Cool storage of the solution, below 15 ºC, may lead to formation of crystals, that can, however, be easily dissolved by gentle warming at 25 ºC until dissolution is complete. Shake container gently to ensure homogeneity.

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

6.5 Nature and contents of container

Bottles of colourless glass (type II), sealed with halogen butyl rubber stoppers, containing 500 ml or 1000 ml of solution.

Contents:

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.

Containers are for single use only. Discard container and any unused contents after use.

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

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, electrolytes 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.

1) Compatibility for mixtures using organic phosphate source:

- Glucose: stability has been demonstrated up to a total quantity of 300 g/l of glucose in the mixture.

- Electrolytes: stability has been demonstrated up to a total quantity of

  - 100 mmol/l of sodium

  - 100 mmol/l potassium in the mixture and

  - 20 mmol/l of magnesium (in mixtures not containing lipids) and 10 mmol/l of magnesium (in mixtures containing lipids)

  - 10 mmol/l of calcium (in mixtures not containing lipids) and 7.5 mmol/l of magnesium (in mixtures containing lipids)

- Lipids: stability has been demonstrated up to a total quantity of 60 g/l of lipid emulsion in the mixture.

- Trace elements and vitamins: stability has been demonstrated with multi-trace elements and multi-vitamins up to the standard dosage recommended by the manufacturer of the micronutrient.

2) Compatibility for mixtures using inorganic phosphate source:

a) Lipid containing mixtures:

- Glucose: stability has been demonstrated up to a total quantity of 224 g/l of glucose in the mixture.

- Electrolytes: stability has been demonstrated up to a total quantity of

  - 100 mmol/l of sodium

  - 100 mmol/l potassium in the mixture and

  - 10 mmol/l of magnesium

- 5 mmol/l of calcium

- Lipids: stability has been demonstrated for total quantities of 5 g/l up to 60 g/l of lipid emulsion in the mixture.

- Trace elements and vitamins: stability has been demonstrated with multi-trace elements and multi-vitamins up to the standard dosage recommended by the manufacturer of the micronutrient.

b) Lipid free mixtures:

- Glucose: stability has been demonstrated for total quantities of 136 g/l up to 224 g/l of glucose in the mixture.

- Electrolytes: stability has been demonstrated up to a total quantity of

  - 100 mmol/l of sodium

  - 100 mmol/l potassium in the mixture and

  - 20 mmol/l of magnesium

  - 5 mmol/l of calcium

- Trace elements and vitamins: stability has been demonstrated with multi-trace elements and multi-vitamins up to the standard dosage recommended by the manufacturer of the micronutrient.

Detailed information about the above mentioned additives and the corresponding shelf life of such admixtures can be provided on demand by the manufacturer.

7 MARKETING AUTHORISATION HOLDER

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