

Rx Prescription drug

Total Amino Acids Preparation Designated Drug

PRESCRIPTION ONLY MEDICINE
READ THE LEAFLET CAREFULLY BEFORE USING.
IF YOU HAVE ANY QUESTIONS, ASK YOUR DOCTOR.

AMINIC[®]

CONTRAINDICATIONS (This product is contraindicated in the following patients.)

1. Patients with hepatic coma or possibility of hepatic coma [it is possible to promote amino acid imbalance and aggravate or induce hepatic coma].
2. Patients with serious kidney disorders or azotemia [it is possible to aggravate symptoms due to nitrogen load].
3. Patients with amino acid metabolism abnormality [it is possible to promote amino acid imbalance].

COMPOSITION & DESCRIPTION

1. Composition

This product contains the following ingredients.

Ingredients	Per 1 bag (200mL)
L-Isoleucine	1.820g
L-Leucine	2.580g
L-Lysine acetate	2.000g
L-Methionine	0.880g
L-Phenylalanine	1.400g
L-Threonine	1.500g
L-Tryptophan	0.260g
L-Valine	2.800g
L-Alanine	1.420g
L-Arginine	1.800g
L-Aspartic acid	0.200g
L-Cysteine	0.070g
L-Glutamic acid	0.100g
L-Histidine	1.000g
L-Proline	1.000g
L-Serine	0.340g
L-Tyrosine	0.080g
Glycine	1.400g
Total amino acid content	20.650g
Amino acid concentration	10.325w/v%

Additives	Per 1 bag (200mL)
Sodium bisulfite	0.060g
Glacial acetic acid (pH adjuster)	Proper
Water for injection	Proper

Total nitrogen content	: 15.2mg/mL
Total free amino acid concentration	: 10.035w/v%
Branched chain amino acid concentration	: 35.9w/v%
EAA/NEAA	: 1.71
Electrolytes	
Na ⁺	: <2.9mEq/L
Cl ⁻	: Not contained
CH ₃ COO ⁻	: ca. 80mEq/L

2. Product description

This product is a colorless and clear aqueous solution for injection.

pH	Osmotic pressure ratio
6.8 – 7.8	ca. 3

3. Description Containers

The standard of bag being used is as follows.

	Total capacity of plastic bag
200mL plastic bag	ca. 380mL

(Fill solution with vertical distance of 75 cm)

INDICATIONS

Supply of amino acid in the following conditions:
Hypoproteinemia, malnutrition, pre- and post-operation

DOSAGE AND ADMINISTRATION

Administer into the peripheral vein

Usually 200-400mL is given slowly by an intravenous drip at a time for an adult. The speed of administration is preferably ca.10g amino acids in 60 min. for their utilization in the body, usually on the standard of 200mL in ca. 120 min. for an adult, and more slowly for a child, elderly and serious patient. It may be adjusted properly depending on the age, symptom and body weight. It is desirable to be administered simultaneously with a saccharide infusion for the efficient utilization of amino acids in the body.

Administer into the central vein

Usually 400-800mL is given into the central vein by a continuous drip in a day for an adult by means of total parenteral nutrition. It may be adjusted properly depending on the age, symptom and body weight.

PRECAUTIONS

1. Careful administration (This product should be administered with caution in the following patients.)

- (1) Patients with serious acidosis [it is possible to aggravate acidosis by administration of large dose]
- (2) Patients with congestive heart failure [it is possible to increase cardiac load due to an increase of the circulating blood volume]
- (3) Patients with hyponatremia [Since this product scarcely contains sodium, it is possible to aggravate hyponatremia]

2. Adverse Reactions

Out of a total of 2,668 patients, 16 cases in 12 patients (0.45%) presented adverse reactions including abnormality on laboratory values. The primary reactions were 5 cases of nausea (0.19%), 2 cases of vomiting (0.08%), 2 cases of hepatic functional disorder (0.08%), 1 case of vascular pain (0.04%) and 1 case of chest discomfort (0.04%).

	Frequency is unknown	Less than 5% - 0.1%	Less than 0.1 %
Hypersensitivity*	[Rash, etc.]		
Digestive organs		Nausea	Vomiting
Circulatory organs	[Palpitation]		Chest discomfort
Liver			Hepatic functional disorder
Kidneys			Renal functional disorder
Others	[Chill, Heat, Headache]		Vascular pain
Rapid administration, large dose	[Acidosis]		

* : Discontinue administration if such symptom is observed.

[] : Basing on the adverse reactions which are generally observed in total amino acid preparations.

Inform your doctor in case of any adverse reactions related to drug use.

3. Use in the Elderly

Since the elderly often have a physiological hypofunction, it is advisable to take such measures as the reduction in the administration speed or dose under careful supervision.

4. Use during Pregnancy, Delivery or Lactation

- (1) The product should only be used in pregnant women, women suspected of being pregnant, and nursing mothers, provided that the expected therapeutic benefits are evaluated to outweigh the possible risk of treatment. [Safety of the product in pregnant women and nursing mothers has not been established].
- (2) It is desirous not to administer to women who are nursing. If administration is unavoidable, avoid nursing. [Safety during nursing has not been established].

5. Pediatric Use

Safety in children has not been established [few clinical experiences].

6. Cautions in Use

(1) Before administration

- 1) Crystals may precipitate. In this case, heat the solution to 50-60°C to dissolve the crystals. Then, allow the solution to cool down to about the body temperature, and use it.
- 2) Don't use if the solution is not completely clear.
- 3) Use immediately after unpacking, and discard any remainder.

(2) During administration

The product contains about 80mEq/L of acetic acid. In case of a large dose or combination with an electrolyte solution, therefore, be careful about the electrolyte balance.

(3) Administration speed

Administer slowly into the vein.

DRUG INTERACTIONS

Scientific data is not available.

CLINICAL STUDIES

1. General Clinical Studies

AMINIC was administered to 243 patients with operation requiring TPN, infective disease, injury, burn and advanced cancer for more than 1 week. The percentage of effectiveness (more than effective) according to the evaluation for the improvement of nutritional status (objective and subjective symptoms, somatometry, protein nutritional indices) is 99.3% (189/191) in adult and 100% (52/52) in pediatric, respectively, thus the efficacy for severe hypercatabolic at the surgical stress was confirmed.

2. Comparative clinical studies¹⁾

The clinical comparative studies were conducted to 80 patients after the operation of subtotal or total gastrectomy with the commercially available total amino acid preparation as a control. As the results of overall judgement considering daily changes of the protein nutritional indices (total protein, albumin, retinol-binding protein, prealbumin, transferrin), cumulative nitrogen balance etc., it was concluded that AMINIC is more useful and superior in protein metabolism efficiency for hypercatabolism as compared with the conventional amino acid preparation being marketed.

PHARMACOLOGY^{2),3)}

In surgical stress model rats and beagles, it was observed that AMINIC had blood biochemical indices such as serum protein level well maintain, and had nitrogen balance, synthesis of body protein and healing of wound improve.

PHARMACOKINETICS

Adult patients who underwent surgery and needed nutritional support were treated with AMINIC, which was administered at 600 to 800 mL once daily via total parenteral nutrition from the 1st postoperative day. The nutritional treatment was provided for at least 2 weeks in principle. No food intake was allowed for 1 week of treatment, followed by energy supply of at least 70% of total caloric intake via the intravenous route for 1 week. The plasma concentration of branched chain amino acids was maintained at a high level from the 2nd to the 14th postoperative day and returned to the baseline level on the day after discontinuation of AMINIC treatment. In particular, the plasma level of valine increased significantly from the 2nd postoperative day ($P<0.001$) and surpassed the upper limit of the normal range. In contrast, the plasma concentrations of isoleucine and leucine increased within the normal range although the increase was significant for the former from the 2nd ($P<0.05$) and 3rd ($P<0.001$) postoperative days and for the latter from the 3rd postoperative day ($P<0.001$) until the 14th postoperative day. The ratios of essential amino acids to non-essential amino acids, branched chain amino acids to total amino acids, and branched chain amino acids to aromatic amino acids were all significantly high during treatment ($P<0.001$). The plasma levels of glutamic acid and phenylalanine increased above the normal range while that of glutamine was below the normal range. Changes in the plasma concentrations of other amino acids remained in the normal range.

STORAGE AND HANDLING

1. Cautions

- (1) Air-needle is not needed.
- (2) Do not unpack until ready for use in order to prevent solution from coloration. (An oxygen absorber is enclosed in order to keep the stability of the product.)
- (3) Do not use in case the solution, normally clear, becomes colored, or if leak of solution or waterdrops are found inside of the overwrap.
- (4) Do not use in the case that film sealing on the rubber stopper is peeled off.
- (5) Insert the injection needle straight at the O-marked point on the rubber stopper. If the needle is inserted diagonally, it may penetrate the container and cause a leak.
- (6) Handle with care the overwrap because solution becomes colored, if it is damaged.
- (7) Read measures on the container as a reference.
- (8) AMINIC cannot be administered by the tandem system using a connecting U-shaped tube. If two plastic bags of this product are used at the same time or sequentially, use a Y-shaped transfusion set.

2. Storage

Store at temperature between 1°C - 30°C.

PACKAGING

200mL x 30 bags (plastic bag)

Specifications: Manufacturer's

EXPIRATION DATE

Shelf-life: 36 months from the manufacturing date.

The product should be used before the expiration date specified on the outer package and label.

REFERENCE

- 1) Shozo Mori et al. : Jpn. Pharmacol. Ther. 14(10),6341, 1986
- 2) Takeo Kikuchi et al. : Jpn. Pharmacol. Ther. 14(10),6145, 1986
- 3) Takao Fujimura et al. : Jpn. Pharmacol. Ther. 14(10),6135, 1986

Follow exactly your physician's prescription

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