For the use of Registered Medical Practitioner or Hospital or a Laboratory only

L-Alanyl L-Glutamine Solution For Infusion (20% w/v)
L-GLUTANIR™*

DESCRIPTION

L-GLUTANIR™* Contains L-Alanyl L-Glutamine for Intravenous infusion.
L-Alanyl L-Glutamine Injection is a clear, colorless solution.
Each 100 mL of concentrated solution for
Infusion contains:

N (2)-L-Alanyl L-Glutamine	20.00 gm
(L-Alanine 8.20 g L-Glutamine 13.46 g)	
Water for Injections IP	q. s. to 100 ml
Theoretical Osmolarity	921 mosmol/l
Titration acidity	90-105 mmol NaOH/l
pH value	5.4-6.0

Pharmacodynamics

The dipeptide N(2)-L-Alanyl L-Glutamine is endogenously split into the amino acids glutamine and alanine hereby supplying glutamine with infusion solutions for parenteral nutrition. The released amino acids flow as nutrients into their respective body pools and are metabolised according to the needs of the organism. Many disease conditions, in which parenteral nutrition is indicated, are accompanied by a glutamine depletion, which glutamine containing infusion regimens counteract.

Pharmacokinetics

N(2)-L-Alanyl L-Glutamine is rapidly split into alanine and glutamine after infusion. In man, half-lives of between 2.4 min and 3.8 min (in terminal renal insufficiency 4.2 min) and a plasma clearance of between 1.6 min and 2.7 L/min were determined. The disappearance of the dipeptide was accompanied by an equimolar increase of the corresponding free amino acids. Hydrolysis probably takes place exclusively in the extracellular space. Renal elimination of N(2)-L-Alanyl L-Glutamine under constant infusion is below 5% and thus the same as that of infused amino acids.

INDICATIONS

L-GLUTANIR™* is indicated as part of a clinical nutrition regimen in patients in hypercatabolic and/or hypermetabolic states. It should be given together with parenteral or enteral nutrition or a combination of both.

DOSAGE AND ADMINISTRATION

For central venous infusion after addition to a compatible infusion solution.
Solutions of mixtures with an osmolarity above 800 mOsmol/L should be infused by the central venous route.

Adults:

L-GLUTANIR™* is administered parallel with parenteral nutrition or enteral nutrition or a combination

of both. Dosege depends on the severity of the catabolic state and on amino acid/protein requirement. A maximum daily dose of 2 g amino acids/kg body weight should not be exceeded in parenteral nutrition. The supply of alanine and glutamine via L-GLUTANIR™*should be taken into consideration in the calculation; the proportion of the amino acid supplied through L-GLUTANIR™* should not exceed approx. 30% of the total supply.

Daily dose
1.5-2.5 ml of L-GLUTANIR™* per kg body weight (equivalent to 0.3 – 0.5 g N(2)-L-Alanyl L-Glutamine per kg body weight). This equates to 100 to 175 ml L-GLUTANIR™* for a patient of 70 kg body weight.

Maximum daily dose: 2.5 ml equivalent to 0.5 g N(2)-L-Alanyl L-Glutamine of L-GLUTANIR™* per kg body weight.

The maximum daily dose of 0.5 g N(2)-L-alanyl-L-glutamine per kg body weight should be administered in combination with at least 1.0 g amino acids/protein per kg body weight per day. With amino acids from L-GLUTANIR™* included these results in a daily dosage of at least 1.5 g amino acids/protein per kg body weight.

The following adjustments are examples for the supply with L-GLUTANIR™* and amino acids through the parenteral nutrition solution, and/or protein through enteral nutrition formula:

Amino acids/protein requirement 1.2 g/kg body weight per day:
0.8 g amino acids/protein + 0.4 g N(2)-L-glutamine per kg body weight

Amino acids/protein requirement 1.5 g/kg body weight per day:
1.0 g amino acids/protein + 0.5 g N(2)-L-alanyl-L-glutamine per kg body weight

Amino acids/protein requirement 2 g/kg body weight per day:
1.5 g amino acids/protein + 0.5 g N(2)-L-alanyl-L-glutamine per kg body weight.

L-GLUTANIR™* is an infusion solution concentrate which is not designed for direct administration

<u>Patients with total parenteral nutrition</u>
The rate of infusion depends on that of the carrier solution and should not exceed 0.1 g amino acids/kg body weight per hour.

L-GLUTANIR™* should be mixed with a compatible amino acid carrier solution or an amino acid containing infusion regimen prior to administration.

<u>Patients with total enteral nutrition</u>
L-GLUTANIR™* is continuously infused over 20-24 hours per day. For peripheral venous infusion, dilute L-GLUTANIR™* to an osmolarity ≤ 800 mosmol/L (e.g. 100 mL L-GLUTANIR™* +100 mL saline).

<u>Patients with combined enteral and parenteral nutrition</u>
The full daily dosage of L-GLUTANIR™* should be administered with the parenteral nutrition, i.e. mixed with a compatible amino acid solution or an amino acid contained in infusion regimen prior to

administration.

Duration of administration
The duration of use should not exceed 3 weeks.

Children
Safety and efficacy in children have not been established.

CONTRAINDICATIONS
L-GLUTANIR™* should not be administered to patients with severe renal insufficiency (creatinine clearance < 25 ml/min), severe hepatic insufficiency, severe metabolic acidosis or known hypersensitivity to the active substances or to any of the recipients.

WARNINGS AND PRECAUTIONS
It is advisable to regularly monitor liver function parameters in patients with compensated hepatic insufficiency.

Serum electrolytes, serum osmolarity, water balance, acid-base status as well as liver function tests (alkaline phosphatase, ALT, AST), possible symptoms of hyperammonaemia should be controlled.

The enzymes alkaline phosphatase, GPT, GOT, bilirubin level and the acid-base status should be monitored.

The choice of a peripheral or central vein depends on the final osmolarity of the mixture. The general accepted limit for peripheral infusion is about 800 mOsmol/L but it varies considerably with the age and general condition of the patient and the characteristics of the peripheral veins.

Experience with the use of L-GLUTANIR™* for longer periods than nine days is limited.

Mutagenic and tumorigenic potential:
In vitro and in vivo test gave no indications of mutagenic potential.
Studies investigating the tumorigenic potential were not carried out. Carcinogenic effects are not to be expected.
L-GLUTANIR™* is presumed to be safe or unlikely to produce an effect on the ability to drive or use machinery.

Use in pregnancy and lactation
As there is currently insufficient data on administration of L-Alanyl L-Glutamine to pregnant women, nursing mothers and children, administration of the preparation in these patient groups is not recommended.
Reproduction toxicity: As per literature studied, teratogenic effect on animal is not reported.

ADVERSE REACTIONS
Not known when correctly administered.

INTERACTIONS

No interactions are known to date.

OVERDOSAGE

As with other infusion solutions, chills, nausea and vomiting can occur, when the infusion rate of L-GLUTANIR™* is exceeded. Infusion shall be stopped immediately in this case.

PHARMACEUTICAL PRECAUTIONS

Instructions for use

L-GLUTANIR™* is an infusion solution concentrate which is not designed for direct administration. The container and the solution should be inspected visually prior to use. Use only clear, particle-free solution and undamaged container. For single use only. To be used immediately after the bottle is opened.

The addition of the concentrate to the amino acid solution prior to application should take place under aseptic conditions ensuring that the concentrate is well dispensed. Unused solution should be disposed of.

L-GLUTANIR™* is infused with the carrier solution. For details see Dosage and Administration section

STORAGE

Store below 25° C.
Shelf life: 24 months
Do not use after the expiry date stated on the label.
Any remaining solution from the opened container must be discarded.

PACKAGE QUANTITIES

Glass bottles of 50 mL &100 mL

ACULIFE®

Manufactured in India by:
Aculife Healthcare Pvt. Ltd.
Sachana, Gujarat 382150, India.

* TM owners-Nirma Ltd.