PROFESSIONAL INFORMATION

SCHEDULING STATUS: S 3

1. NAME OF THE MEDICINE

DIPEPTIVEN (Concentrate for solution for infusion)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

100 mL contains:

N(2)-L-alanyl-L-glutamine	20 g which provides
L-alanine	8,20 g
L-glutamine	13,46 g

Sugar free

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Concentrate for solution for infusion.

A clear solution in glass bottles containing 50 mL or 100 mL.

Theoretical osmolarity	921 mOsm/L
pH-value	5,4 - 6,0

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

DIPEPTIVEN is indicated as part of an intravenous parenteral nutrition regimen as a supplement to amino acid solutions which do not already contain glutamine.

4.2 Posology and method of administration

Posology

DIPEPTIVEN IS AN INFUSION SOLUTION CONCENTRATE WHICH IS NOT DESIGNED FOR DIRECT ADMINISTRATION.

The duration of use should not exceed 2 weeks.

Adults

Dosage depends on the severity of the catabolic state and on amino acid requirement.

A maximum daily dosage of 2 g amino acids per kg body weight should not be exceeded in parenteral nutrition. The supply of alanine and glutamine via DIPEPTIVEN should be taken into consideration in the calculation: the proportion of the amino acids supplied through DIPEPTIVEN should not exceed approximately 30 % of the total supply.

Daily Dose:

1,5 – 2,5 mL DIPEPTIVEN 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 DIPEPTIVEN 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 DIPEPTIVEN 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 per kg body weight per day. With the amino acids from DIPEPTIVEN included, this results in a daily dosage of at least 1,5 g amino acids per kg body weight.

The following adjustments are examples for the supply with DIPEPTIVEN and other amino acids through the carrier solution:

Amino acids requirement 1,2 g/kg body weight per day:

0,8 g amino acids + 0,4 g N(2)-L-alanyl-L-glutamine per kg body weight.

Amino acids requirement 1,5 g/kg body weight per day:

1,0 g amino acids + 0,5 g N(2)-L-alanyl-L-glutamine per kg body weight.

Amino acids requirement 2 g/kg body weight per day:

1,5 g amino acids + 0,5 g N(2)-L-alanyl-L-glutamine per kg body weight.

Special populations

Children

Safety and efficacy in children have not been established.

Method of administration

DIPEPTIVEN is designed for central venous infusion following ADDITION TO A COMPATIBLE CARRIER SOLUTION.

Patients with total parenteral nutrition

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.

DIPEPTIVEN should be mixed with a COMPATIBLE amino acid carrier solution or an amino acid containing infusion regimen prior to administration.

Refer to section 6.6 for special precautions for disposal and other handling procedures.

4.3 Contraindications

DIPEPTIVEN should not be administered to patients with:

- Hypersensitivity to N(2)-L-alanyl-L-glutamine, or to any of the excipients of DIPEPTIVEN listed in section 6.1;
- Renal or hepatic insufficiency;
- Metabolic acidosis;
- Circulatory shock;
- Hypoxia;
- Multiple organ failure;
- Pregnancy and lactation, as the safety has not been demonstrated;
- Children, as the safety has not been demonstrated.

4.4 Special warnings and precautions for use

For a safe administration the maximum dose of DIPEPTIVEN should not exceed 2,5 mL (corresponding to 0,5 g N(2)-L-alanyl-L-glutamine) per kg body weight per day (see sections 4.2, 4.9 and 5.1).

DIPEPTIVEN should only be used as part of clinical nutrition, and its dosage is limited by the amount of protein/amino acids provided by nutrition (see section 4.2). Whenever the clinical condition does not allow nutrition (e.g., circulatory shock, hypoxia, unstable critically ill patients, severe metabolic acidosis) DIPEPTIVEN should not be administered.

Oral/enteral intake of glutamine-supplemented formulas in combination with parenteral nutrition should be taken into consideration for calculation of the prescribed dose of DIPEPTIVEN.

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

Serum electrolytes, serum osmolarity, fluid balance, acid-base status, creatinine clearance, urea, as well as liver function tests (alkaline phosphatase, ALT, AST, bilirubin) and possible symptoms of hyperammonaemia should be monitored.

4.5 Interaction with other medicines and other forms of interaction

No interactions have been reported.

Incompatibilities: DIPEPTIVEN must not be mixed with other medicines except those mentioned under “Method of administration” (see section 4.2).

4.6 Fertility, pregnancy and lactation

The use of DIPEPTIVEN is contraindicated in pregnancy and lactation (see section 4.3)

4.7 Effects on ability to drive and use machines

It is unlikely that DIPEPTIVEN would produce an effect on the ability to drive or use machinery.

4.8 Undesirable effects

Chills, nausea and vomiting can occur when the infusion rate of DIPEPTIVEN is exceeded. Infusion must be stopped immediately in such a case.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

Healthcare providers are asked to report any suspected adverse drug reactions to the Holder of the Certificate of Registration at the following email address: safety.fksa@fresenius-kabi.com and to the relevant medicine's regulatory authority in the country where the product is marketed.

4.9 Overdose

Refer to "Undesirable effects" in section 4.8 above. Treatment is symptomatic and supportive.

Experience from a study in critically ill patients with at least two organ failures at admission, receiving the maximum approved daily intravenous infusion of DIPEPTIVEN (0,5 g alanyl-glutamine/kg/day) together with a high dose of enteral glutamine (30 g) provided as a mixture of alanyl-glutamine and glycyl-glutamine and without appropriate clinical nutrition, has shown an increase in serious side effects.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacological classification: A 23 Amino acids

Pharmacotherapeutic group: Amino acids – concentrate for solution for parenteral nutrition

ATC code: B05X B02

Concentrate of the Dipeptide N(2)-L-alanyl-L-glutamine, is designed to be used to supply glutamine during parenteral nutrition.

In a large multicenter study, critically ill adult patients with at least two organ failures at admission and requiring mechanical ventilation received either supplemental glutamine alone, antioxidants, glutamine and antioxidants, or placebo. In the glutamine groups, patients concomitantly received parenteral and enteral glutamine in their maximally allowed amounts exceeding the recommended dose by two-fold. Overall, mortality for the entire study population at 28 days, the primary endpoint, was not statistically significantly different between the groups. However, 6-month mortality, in a retrospective analysis, was tendentially increased in patients receiving the combined very high total dose of glutamine during unresuscitated shock and renal failure; glutamine and nutrition should not be used in unresuscitated shock

accompanied by renal failure (see section 4.9). Under these specific circumstances the patient's ability to metabolise glutamine seems to have been exceeded (see also section 4.4).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for injection

6.2 Incompatibilities

This medicine must not be mixed with other medicines except those mentioned in section 6.6.

6.3 Shelf life

24 months.

To be used immediately after the bottle is opened.

DIPEPTIVEN is not to be stored after addition of other components.

6.4 Special precautions for storage

Store at or below 25 °C.

6.5 Nature and contents of container

10 x 50 mL glass bottles.

10 x 100 mL glass bottles.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

DIPEPTIVEN is an infusion solution concentrate which is not designed for direct administration. DIPEPTIVEN is infused with the carrier solution.

One volume part DIPEPTIVEN is to be mixed with at least 5 volume parts carrier solution (e.g. 100 mL DIPEPTIVEN + at least 500 mL amino acid solution). The maximum final concentration should not exceed 3,5 %.

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.

The addition of the concentrate to the carrier solution prior to application should take place under aseptic conditions. Thorough mixing and compatibility must be ensured. Use immediately after dilution and dispose of any unused solution.

FURTHER MEDICINES SHOULD NOT BE ADDED TO THE MIXTURE.

7. HOLDER OF THE CERTIFICATE OF REGISTRATION

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8. REGISTRATION NUMBER

33/23/0210

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

09 November 2000

10. DATE OF REVISION OF THE TEXT

09 May 2025

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