* Revised: April 2024 (2nd version)
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Standard Commodity Classification No. of Japan:
873253

Comprehensive amino acid preparation for high-calorie infusion for Pediatrics

Storage : Store at room temperature
Expiration date: 3 years

Prescription drug:
(Caution – Use only pursuant to the prescription issued of physician, etc.)

Pleamin-P Injection "FUSO"

Approval No.	20700AMZ00524
Date of initial marketing in Japan	July 2004

2. CONTRAINDICATIONS (Do not administer to the following patients.)

2.1 Patients with aberrant amino acid metabolism [There is a risk that the administered amino acids will not be metabolised, and that amino acid imbalance will be exacerbated.]

2.2 Patients with severe renal dysfunction or azotemia (both except for patients undergoing dialysis or hemofiltration) [see 8., 9.2.1, 9.2.2]

2.3 Patients with hepatic coma or those at risk of hepatic coma [see 9.3.1]

3. COMPOSITION AND PRODUCT DESCRIPTION

3.1 **Composition**

Product name	Pleamin-P Injection "FUSO"	
Volume	200 mL	
Active Ingradients	In one bag,	
	L-Isoleucine	1,600 mg
	L-Leucine	3,200 mg
	L-Lysine acetate	1,354 mg
	L-Methionine	300 mg
	L-Phenylalanine	500 mg
	L-Threonine	480 mg
	L-Tryptophan	240 mg
	L-Valine	1,200 mg
	L-Arginine	2,000 mg
	L-Histidine	500 mg
	Glycine	400 mg
	L-Alanine	1,040 mg
	L-Glutamic acid	160 mg
	L-Aspartic acid	160 mg
	L-Proline	1,200 mg
	L-Serine	800 mg
	L-Tyrosine	120 mg
	L-Cysteine	300 mg
	Taurine	40 mg
Inactive Ingredients	In one bag,	
	Sodium hydrogen sulfite	60 mg
	pH adjuster	

Total free amino acid content : 7,600 mg/100 mL
Essential amino acid content (E) : 4,490 mg/100 mL
Non-essential amino acid content (N) : 3,110 mg/100 mL
E/N : 1.44

Total nitrogen content : 1,175 mg/100 mL
Branched-chain amino acid content (%) : 39%

Electrolyte level:
Na^+ : approximately 3 mEq/L
CH_3COO^- : approximately 80 mEq/L

3.2. Product Description

Product name	Pleamin-P Injection "FUSO"
Dosage form	Aqueous injection
Appearance	Clear and colorless liquid
pH	6.5 – 7.5
Osmotic pressure ratio (ratio to saline)	2.3 – 2.8

4. INDICATIONS

Pleamin-P Injection is indicated for amino acid supplementation in neonates (weighing ≥ 2 kg at birth, in principle), infants, and pediatrics in the following conditions: hypoproteinemia, malnutrition, and before and after operation.

6. DOSAGE AND ADMINISTRATION

The usual recommended dosage of Pleamin-P Injection for total parenteral nutrition is 23-36 mL (equivalent to 1.75-2.75 g amino acids) per kg per day for neonates weighing ≥ 2 kg at birth and infants; 20-33 mL (equivalent to 1.50-2.50 g amino acids) per kg per day for children aged 1-3 years. All doses should be administered by continuous intravenous infusion.
The dosage may be modified according to patients' symptoms and laboratory data.

8. IMPORTANT PRECAUTIONS

8.1 The amount of urea and other substances removed and the amount accumulated in patients with severe renal impairment or patients with hypernitrosemia undergoing dialysis or hemofiltration will differ depending on the dialysis method and the patient's condition. The patient's condition should be confirmed by evaluating blood biochemistry, acid-base balance, and fluid balance, etc., before deciding whether to start or continue treatment. [See 2.2, 9.2.2]

8.2 During total parenteral nutrition, particularly in its early phase, AST and ALT may show small transient elevations. In such cases, the patient's symptoms and laboratory data should be monitored carefully, and reducing the dose (or energy intake) until acclimatization should be considered.

9. PRECAUTIONS CONCERNING PATIENTS WITH SPECIFIC BACKGROUNDS

9.1 Patients with complications, past medical history, etc.

9.1.1 Patients with severe acidosis
There is a risk of worsening acidosis.

9.1.2 Patients with congestive cardiac failure
There is a risk that symptoms may worsen due to an increase in circulating blood volume.

9.1.3 Patients with hyponatremia
There is a risk of worsening hyponatremia.

9.2 Patients with renal impairment

9.2.1 Patients with severe renal impairment or patients with hypernitremia (except for patient undergoing dialysis or hemofiltration)
Do not administer. There is a risk that the accumulation of urea and other metabolites of amino acids may worsen the condition. [See 2.2]

9.2.2 Patients with severe renal impairment or hypernitrosemia undergoing dialysis or hemofiltration
There is a risk that the accumulation of urea and other metabolites of amino acids may occur. [See 2.2, 8.1]

9.3 Patients with hepatic dysfunction

9.3.1 Patients with hepatic coma or those at risk of hepatic coma
Do not administer. There is a risk that symptoms may worsen or be induced due to insufficient amino acid metabolism. [See 2.3]

9.7 Pediatric use

The product can be administered to infants weighing < 2 kg at birth only if the expected therapeutic benefits outweigh the possible risks associated with treatment and only with care using a dosage modified according to their symptoms and laboratory data.

11. ADVERSE REACTIONS

The following adverse reactions may occur, so please monitor the patient closely and take appropriate measures such as discontinuing the drug if any adverse reactions are observed.

11.2 Other adverse reactions

	0.1-<5%	Incidence unknown
Hypersensitivity		Rash
Gastrointestinal		Nausea and vomiting
Cardiovascular		Chest discomfort and palpitations
Hepatic	Increased AST, ALT, and/or ALP.	Jaundice (increased bilirubin)
Massive/rapid infusion		Acidosis
Miscellaneous		Chills, pyrexia, and headache

14. PRECAUTIONS CONCERNING USE

14.1 General Precautions

14.1.1 Take precautions against infection when using.

14.1.2 When inserting a needle into a rubber stopper, such as an injection needle or a bottle needle for an infusion set, insert it slowly and vertically into the indentation on the rubber stopper. If you insert it at an angle, there is a risk that shavings may get mixed in or cause a leak. Also, do not repeatedly insert the needle into the same spot.

14.2 Precautions when preparing medicines

When mixing medicines, be careful of any changes in the mixture.

14.3 Precautions for Administering the Solution

14.3.1 Since the product contains acetate at about 80 mEq/L, pay attention to the electrolyte homeostasis when infusing a massive volume of the product or infusing it in combination with an electrolyte fluid.

14.3.2 Slowly infuse the product intravenously.

14.3.3 In principle, do not administer using a tandem method with a connecting tube. There is a risk of air entering the infusion set.

14.3.4 Use the graduations on the infusion bag only to make a rough estimate of the volume administered.

14.3.5 Never use the solution from a previously opened bag.

16. PHARMACOKINETICS

16.3 Distribution

When male SD rats, 3 weeks old, were given a 90-min continuous intravenous infusion of this product with the 19 amino acids labeled with 14C, the distribution rate to the organs was particularly high in the liver immediately after the end of administration and for 5 hours, followed by the pancreas, kidneys and brain. [1)]

16.5 Excretion

When male SD rats, 3 weeks old, were given a 90-min continuous intravenous infusion of this product with the 19 amino acids labeled with 14C, approximately 46% of the administered radioactivity was excreted in the breath, approximately 5% in the urine, and approximately 6% in the faeces by day 7.[1)]

17. CLINICAL STUDIES

17.1 Clinical Studies for Efficacy and Safety

17.1.1 Phase III study in Japan

A randomised controlled trial was conducted in 160 neonatal and infant patients requiring nutritional management with high-calorie infusion therapy. The study drug or the control drug was mixed to achieve a target maintenance amino acid dose of approximately 2.5 g/kg/day, and was administered by continuous intravenous infusion for 7 days. As a result, based on the results of nutritional efficacy, weight gain, nitrogen balance, plasma protein and plasma amino acid profiles, the study drug was assessed as being effective or more effective in 53 out of 57 cases (93%). The incidence of adverse reactions was 4.7% (3/64 cases), with the main adverse reactions being increased ALT 4.7% (3/64 cases), increased AST 3.1% (2/64 cases), and increased Al-P 1.6% (1/64 cases).[2)]

17.1.2 Clinical trials in Japan

An open study was conducted on 59 neonatal, infant and young child patients who required nutritional management using high-calorie parenteral nutrition. The maintenance dose of amino acids in this study was 2.5 g/kg/day for neonates and infants, and 2.0 g/kg/day for young children, and was administered by continuous intravenous infusion for at least 7 days. As a result, based on the results of nutritional efficacy, weight gain, nitrogen balance, plasma protein and plasma amino acid profiles, 49 out of 53 cases (92%) were assessed as being effective or more, and no side effects were observed.[3)]

17.2 Post marketing Surveillance, etc.

17.2.1 Post marketing study

In the post-marketing surveillance, 27 cases (2.7%) of adverse reactions were reported out of 994 cases. The main types of adverse reactions were: increased AST in 9 cases (0.9%), increased ALT in 6 cases (0.6%), hepatic dysfunction in 6 cases (0.6%), and increased direct bilirubin in 4 cases (0.4%).

17.2.2 Post marketing study of low birth weight infants

Of the 994 cases collected in the post-marketing surveillance, 293 cases were low birth weight infants with a birth weight of less than 2kg, and adverse reactions were reported in 10 cases (3.4%). The main types of adverse reactions were increased AST in 4 cases (1.4%), increased direct bilirubin in 3 cases (1.0%), and increased ALT in 2 cases (0.7%).

18. PHARMACOLOGY

18.1 Mechanism of action

This drug shows the effect of supplementing amino acids.

18.2 Plasma level of free amino acids

When Pleamin-P Injection was used for total parenteral nutrition of rats in pre-weaning, weaning and post-weaning periods, the plasma level of free amino acids was more likely to be within or near the normal range in younger rats.[4)]

18.3 Nutritional effect

When Pleamin-P Injection was used for total parenteral nutrition of rats, pre-weaning and weaning rats gained weight in a dose-dependent manner, and weaning rats achieved positive nitrogen balance.

20. PRECAUTIONS FOR HANDLING

20.1 Avoid strong impacts or contact with sharp objects, as it may cause leakage.

20.2 To maintain quality, the product is packaged in a gas-barrier outer bag and contains a desiccant, so please do not open the outer bag until you are ready to use it.

20.3 Check the colour of the indicator (oxygen detector) before opening the outer bag, and do not use it if it is blue-violet to blue.

20.4 Do not expose the product under direct sunlight so as to keep the indicator's function normal.

20.5 Do not use the product in the following cases.

- If the outer bag is damaged
- If there are any water droplets or crystals on the surface of the container or inside the outer bag
- If the liquid is leaking from the container
- If there are any crystals that do not dissolve even when the container is shaken
- If there are any abnormalities in the properties or other aspects of the liquid
- If the seal on the rubber stopper has come off

22. PACKAGING

200mL, 10 bags (with oxygen detector/oxygen absorber)

23. REFERENCES

1) Kuroda S, et al.: *Jpn Pharmacol Ther*. 19, 3161, 1991.
2) Okada T, et al.: *Jpn J Parenter Enteral Nutr*. 14, 561, 1992.
3) Okada T, et al.: *Jpn J Parenter Enteral Nutr*. 14, 595, 1992.
4) Tanaka S, et al.: *Jpn Pharmacol Ther*. 19, 3125, 1991.

24. REFERENCE REQUEST AND CONTACT INFORMATION

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26. MARKETING AUTHORIZATION HOLDER, etc

26.1 Marketing Authorization Holder

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