(2015.02.10)
Revised: February 2015 (2nd version)

- AMINO ACID INJECTION -

KIDMIN® IV infusion

< 7.2% Amino Acid IV infusion for Renal Failure >

Prescription Drug
Caution: Use only as directed by a physician.

Storage
Store at temperature not exceeding 30°

Expiration date
Do not use after the expiration date indicated on the container.

KIDMIN IV infusion	250-mL bottle	500-mL bottle
Date of initial marketing in Japan	September 1996	

CONTRAINDICATIONS (KIDMIN Injection is contraindicated in the following patients.)

(1) Patients with hepatic coma or a risk of hepatic coma
[Administration may enhance amino acid imbalance and hepatic coma may be worsened or induced.]

(2) Patients with hyperammonemia
[Because of excess load of nitrogen, hyperammonemia may be worsened.]

(3) Patients with inherited abnormal amino acid metabolism
[Because the infused amino acids are not adequately metabolized, the patient's clinical condition may be worsened.]

DESCRIPTION

1. Composition

Each 100 ml contains :

Item	Content/100 ml
Active ingredients:	
L-Arginine	0.450gm
L-Histidine	0.350gm
L-Isoleucine	0.900gm
L-Leucine	1.400gm
L-Lysine acetate	0.710gm
Eq. to L-Lysine	0.500gm
L-Methionine	0.300gm
L-Phenylalanine	0.500gm
L-Threonine	0.350gm
L-Tryptophan	0.250gm
L-Valine	1.000gm
L-Tyrosine	0.050gm
L-Proline	0.300gm
L-Serine	0.300gm
L-Alanine	0.250gm
L-Cysteine	0.100gm
L-Aspartic acid	0.100gm
L-Glutamic acid	0.100gm
Inactive ingredients:	

Inactive ingredients
Glacial acetic acid
Sodium metabisulphite ($Na_2S_2O_5$)
Water for injection

2. Product Description

KIDMIN IV infusion is a clear and colorless solution .

INDICATIONS

KIDMIN IV infusion is indicated for the provision of amino acids in the following instances in patients with acute or chronic renal failure: hypoproteinemia, malnutrition, before and after surgery and during hemodialysis.

DOSAGE AND ADMINISTRATION

Chronic Renal Failure

1) Peripheral vein infusion

The usual adult dose is 250 mL per day, infused via a peripheral vein. The usual infusion rate in adults is 100 mL over 60 min and it should be slowly infused in elderly, seriously ill patients and in children if there is a medical need and under medical supervision . The dose may be adjusted according to the patient's condition, body weight, and age.

When administered during hemodialysis, it should be infused via the vein side injection port of dialysis circuit starting 90–60 min before the end of hemodialysis therapy. Regarding calories, more than 1500 kcal per day is recommended to be provided for the efficiency of amino acid utilization.

2) Central vein infusion

The usual adult dose is 500 mL per day, infused via a central vein by total parenteral nutrition. The dosage may

be adjusted according to the patient's condition, body weight, and age. More than 300 kcal of nonprotein calories should be administered per 1 g of nitrogen (100 mL of this product) for the efficiency of amino acid utilization.

Acute Renal Failure

The usual adult dose is 500 mL per day, infused via a central vein by total parenteral nutrition. The dose may be adjusted according to patient's condition, body weight, and age. More than 300 kcal of nonprotein calories should be administered per 1 g of nitrogen (100 mL of this product) for the efficiency of amino acid utilization.

< Precautions >

(1) Because it has been reported that hyperammonemia or consciousness disorder occurred when an amino acid injection for renal failure was administered as the sole amino acid source, discontinue use of this product immediately when abnormalities including slow reaction to being called or greetings, or reduction in spontaneous motor activity or expressing opinions are observed.

(2) Because azotemia or metabolic acidosis may be enhanced in case of inadequate administration of calories, the patients must be carefully observed during administration. If abnormalities are found, institute appropriate measures such as withdrawing administration.

PRECAUTIONS

1. Careful Administration (KIDMIN IV infusion should be administered with care in the following patients.)

(1) Patients with cardiovascular dysfunction [An increase in the circulating blood volume may worsen the patient's clinical condition]

(2) Patients with hepatic disorders or gastrointestinal bleeding
[Excess accumulation of amino acids or hyperammonemia may be induced.]

(3) Patients with severe electrolyte imbalance or abnormal acid-base balance
[The patient's clinical condition may be worsened.]

2. Important Precautions

This product should be used in patients who need parenteral nutrition because oral or enteral nutrition is inadequate or not possible.

3. Adverse Reactions

Of a total of 2964 patients evaluated, 122 adverse reactions including laboratory abnormalities were reported in 74 patients (2.5%) (data at the time of reexamination, 2007, Japan). If adverse reactions are observed, institute appropriate measures such as withdrawing administration.

Reactions	Frequency unknown	<0.1%	0.1% –<5%
Hypersensitivity	[Rash]		
Gastrointestinal			Nausea, Vomiting
Cardiovascular	[Chest discomfort, palpitation]		
Hepatic			Abnormal liver function test values (increases in AST (GOT), ALT (GPT), gamma-GTP, ALP, LDH, LAP, or total bilirubin), hyper-ammonemia
Renal			Increases in blood urea nitrogen or creatinine
Large dose and rapid administration	[Acidosis]		
Other	[Chills, fever, feeling of warmth, vascular pain]	Lower extremity edema, dry mouth, headache	Hyper-potassemia

4. Use in the Elderly

Because elderly patients often have reduced physiological function and are likely to develop hepatic or cardiovascular dysfunction, it is advisable to consider reducing the dose by decreasing the infusion rate.

5. Use during Pregnancy, Delivery, or Lactation

The safety in pregnant women has not been established. Therefore, this product should be used in pregnant women and women who may possibly be pregnant only if the expected therapeutic benefits outweigh any possible risk.

6. Pediatric Use:

The safety of Kidmin IV infusion in children has not been established (insufficient clinical experience)

(1) Physiological system for the metabolism of various amino acids may not be fully developed in children It is therefore advisable to take special precautions such as reducing the infusion rate when administering Kidmin infusion to pediatric patients.

(2) Kidmin infusion may induce hyperkalemia in low birth weight infants. If hyperkalemia develops , discontinue Administration and take appropriate measures to reduce serum potassium levels.

7. Precautions Concerning Use

(1) At the time of preparation

Physicochemical changes of the solution such as precipitation may occur when this product is combined with the following drugs. Changes should be observed.

a) Drugs which are designed to be stable in alkaline conditions.

b) Drugs which are not soluble in water.

(2) Before administration

1) To minimize the risk of infection, carry out all procedures under aseptic conditions.

2) In cold environmental conditions, the solution should be warmed to near body temperature before use.

3) Use the solution immediately after opening the container. After use, discard all unused solution.

(3) During administration

1) Because the solution contains approximately 46 mEq/L of acetate, a large dose or concomitant use with an electrolyte solution requires careful monitoring of electrolyte balance.

2) Administer the solution slowly via vein.

PHARMACOKINETICS

(Reference data in rats):

When ^{14}C-labeled KIDMIN IV infusion was infused to normal 12-week-old rats and to 7/8 nephrectomized rats by TPN, the radioactivity was rapidly distributed throughout the body, with 50–90% incorporation to the protein fractions of the plasma, muscle, and major organs such as liver, kidney, and pancreas from 3 to 72 hr after infusion. The expiratory excretion relative to the administered radioactivity was 32% in normal rats and 34% in nephrectomized rats up to 72 hr after infusion and the urinary excretion relative to the administered radioactivity was 4.6% and 4.9%, respectively.[1)]

CLINICAL STUDIES

Clinical trials were conducted in 218 patients with acute or chronic renal failure, mainly those who needed blood purification treatment, and the following results were obtained.[2–7)]

(1) In the total parenteral nutrition (central vein infusion) in patients in whom oral nutrition was not tolerated, KIDMIN IV infusion showed favorable effects on serum total protein, albumin, and rapid-turnover protein with smaller changes in serum aminograms and alleviated an increase in blood urea nitrgen.[2–5)]

(2) In the peripheral use of KIDMIN IV infusion as a supplement to the oral intake of protein, the nutritional parameters such as serum total protein, transferrin, andVal/Gly ratio were favorably maintained.[6,7)]

PHARMACOLOGY

(1) KIDMIN IV infusion, administered by TPN, exerted the following nutritional effects in chronic renal failure animals (7/8 nephrectomy rats[8,9)] and 7/8 renal artery-ligated dogs[10)]) and acute renal failure animals (mercuric chloride-induced renal failure rats[11)] and total nephrectomy rats[12)]).

1) Favorable body weight gain and nitrogen balance.[8,10,11)]

2) Normalized aminograms in blood and BCAA levels in muscle.[8,10)]

3) Increased uptake of ^{15}N-leucine into blood protein fraction.[9)]

4) Smaller increase in blood urea nitrogen.[12)]

(2) The amino acid-providing effect of KIDMIN IV infusion was studied in 7/8 nephrectomized rats on a low-protein diet,[13)] and the following nutritional effects were observed.

1) Improvement in nutritional status as evidenced by body weight gain, nitrogen balances, and normalized blood aminogram.

2) No increase in blood urea nitrogen.

PRECAUTIONS FOR HANDLING:

(1) Because an oxygen absorbant is enclosed between the bottle and the outer wrap to maintain stability of the solution , do not remove the outer wrap until use

(2) A crystalline precipitate may form due to temperature changes during storage. Shake the solution at temperatures of 15–25°C to dissolve precipitate before use.Excrusions are made up to 30 °C

(3) Do not use the product if the outer wrap covering the product has been damaged, the solution is discoloured or yellowish , the indicator tablet blue discoloured or a precipitate that cannot be dissolved by shaking has formed.

(3) Puncture the rubber stopper vertically with a needle at the place marked with a circle. If the stopper is not punctured vertically, the needle could pass through the neck of the container and cause leakage of the contents. Do not puncture the bottle except at the rubber cap mark

(4) Do not use the solution if there are droplets inside the outer wrap or if the solution is cloudy.

(5) Volume markings on the container may not be accurate. Use them only as a guide.

Store at temperature Not exceeding 30°C to be used immediately after opening.

PACKAGING

KIDMIN IV infusion

250 mL or 500 mL in polyethylene plastic bottle with rubber cap and oxygen indicator tablet is present

N.B. 500mL for tender only

REFERENCES

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REQUEST FOR LITERATURE SHOULD BE SENT TO:

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Report of side effects should be sent to:

Safetyreport@egyptotsuka.com .

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