

See Package Insert for full prescribing information. Following is a brief summary.

5.4% NephAmine® (Essential Amino Acid Injection)

Protect from light until use.

DESCRIPTION

5.4% NephAmine (Essential Amino Acid Injection) is a sterile, nonpyrogenic solution containing crystalline essential amino acids plus histidine. Each 250 mL unit provides Rose's recommended daily intake of essential amino acids¹ plus 625 mg of histidine, considered essential for uremics. The total nitrogen content of a 250 mL unit is approximately 1.6 grams (10 g of protein equivalent) in 14 grams of amino acids. All amino acids designated USP are the "L" isomer.

Each 100 mL contains:

Histidine USP	0.25 g
Isoleucine USP	0.56 g
Leucine USP	0.88 g
Lysine (added as Lysine Acetate USP)	0.64 g 0.90 g
Methionine USP	0.88 g
Phenylalanine USP	0.88 g
Threonine USP	0.40 g
Tryptophan USP	0.20 g
Valine USP	0.64 g
Cysteine (as Cysteine HCl•H ₂ O USP)	<0.014 g <0.020 g
Sodium Bisulfite (as an antioxidant)	<0.05 g
Water for Injection USP	qs

pH adjusted with Sodium Hydroxide NF as required.

pH: 6.5 (6.0-7.0); Calculated Osmolarity: 435 mOsmol/liter

Total Nitrogen: Approx. 0.65 g/100 mL

Concentration of Electrolytes (mEq/liter): Sodium 5, Chloride <3
Acetate Approx. 44

¹ Histidine is considered an essential amino acid in uremic patients.

² Rose WC: The sequence of events leading to the establishment of the amino acid needs of man. *Am J Public Health*; 1968; 58 (11):2020-2027.

INDICATIONS AND USAGE

5.4% NephAmine is indicated for adult and pediatric use, in conjunction with other measures, to provide nutritional support for uremic patients, particularly when oral nutrition is infeasible or impractical. See *Special Precautions in Pediatric Patients* for additional information.

during the first few days of central venous nutrition, to prevent or minimize these complications.

Special Precautions in Patients with Renal Insufficiency

Frequent laboratory studies are necessary in patients with renal insufficiency due to underlying metabolic abnormalities. Hyperglycemia, a frequent complication, may not be reflected by glycosuria in renal failure. Blood glucose, therefore, must be determined frequently, often every six hours to guide dosage of dextrose and insulin if required.

Serum concentrations of potassium, phosphorus, and magnesium may dramatically decline with successful treatment, individually or together; these substances should be supplemented as required. Special care must be taken to avoid hypokalemia in digitalized patients, or those with cardiac arrhythmias.

Special Precautions in Pediatric Patients

5.4% NephAmine (Essential Amino Acid Injection) should be used with special caution in pediatric patients, due to limited clinical experience.

Laboratory and clinical monitoring of pediatric patients, especially when nutritionally depleted, must be extensive and frequent. Initial total daily dose should be low, and increased slowly. Dosage of NephAmine above one gram of essential amino acids per kilogram body weight per day is not recommended.

For neonates and other infants (especially low birth weight infants), amino acid formulations developed specifically for nutritional support of infants and children should be considered. If NephAmine is administered to these very young patients, extra caution in frequent monitoring of plasma amino acid levels and serum ammonia is strongly recommended.

Frequent monitoring of blood glucose is required in neonates, low birth-weight, or septic infants as infusion of hypertonic dextrose carries a greater risk of hyperglycemia in such patients.

The absence of arginine in NephAmine may accentuate the risk of hyperammonemia in infants.

ADVERSE REACTIONS

See **WARNINGS** and *Special Precautions for Central Venous Nutrition*. Reactions which may occur because of the solution or the technique of administration include febrile response, infection at the site of injection, venous thrombosis, and hypervolemia.

Symptoms may result from an excess or deficit of one or more of the ions present in the solution infused, therefore, frequent monitoring of electrolyte levels is essential.

Infrequent instances of hyperammonemia have been reported following administration of essential amino acid solutions to patients with massive gastrointestinal hemorrhage, nonuremic infants and children or following administration of higher than recommended doses to adult or pediatric patients. Elevated plasma amino acid levels (hypermethionemia) have also been reported in infants especially in higher dosage ranges. Elevated serum ammonia levels, plasma amino acid levels, and clinical symptoms may subside when the infusions are discontinued.

Phosphorus deficiency may lead to impaired tissue oxygenation and acute hemolytic anemia. Relative to calcium, excessive phosphorus intake can precipitate hypocalcemia with cramps, tetany, and muscular hyperexcitability.

If an adverse reaction does occur, discontinue the infusion, evaluate the patient, institute appropriate therapeutic countermeasures and save the remainder of the fluid for examination if deemed necessary.

OVERDOSAGE

In the event of a fluid or solute overload during parenteral therapy, reevaluate the patient's condition, and institute appropriate corrective treatment.

Exposure of pharmaceutical products to heat should be minimized. Avoid excessive heat. Protect from freezing. It is recommended that the product be stored at room temperature (25°C); however, brief exposure up to 40°C does not adversely affect the product.

Protect from light until use.

Rx only

Revised: November 2001 (485)

AFFIX BUSINESS CARD STICKER HERE

For Technical Information call: 800-854-6851
For Order Services call: 800-BBRAUN2 (800-227-2862)
Website: www.bbraunusa.com

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5.4% NephAmine® (Essential Amino Acid Injection)

Nutrition Support for the Acute and
Chronic Renal Failure Patient

Formulation (per liter)*

- Provides Rose's recommended intake of essential amino acids¹ plus 625 mg of Histidine.
- Calorie: nitrogen ratio 744:1
- Essential Amino Acids 13.4 g
- Total nitrogen 1.6 g

Usage

- Parenteral therapy management of patients with nutritional deficiencies resulting from acute and chronic renal failure

Benefits

- Increases survival in acute renal failure¹⁻³
- Promotes earlier return of renal function in patients with potentially reversible acute renal failure³
- Decreases rate of rise in BUN levels¹⁻³
- Minimizes electrolyte balance deterioration¹⁻³
- Decreases number of required dialyses¹

Note: Contraindicated in patients with anuria, inborn errors of amino acid metabolism or hypersensitivity to one or more amino acids present in the solution. Frequent evaluation and laboratory determinations are necessary for proper monitoring of parenteral nutrition.

* When admixed with 70% dextrose

¹ Abel RM, et al: *New Eng J Med* 1973

² Freung H, et al: *Surg Gyn Obstet* 1990

³ Feinstein E, et al: *Kidney Int* 1983

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5.4% NephAmine®

(Essential Amino Acid Injection)

Support for the Acute and
Chronic Renal Failure Patient

Adults	1 unit/day	2 units/day
5.4% NephAmine	250 mL	500 mL
70% Dextrose	500 mL	1000 mL
Total Fluid	750 mL	1500 mL
Calorie: Nitrogen ratio	744:1	744:1
Essential Amino Acids (EAA)	13.4 g	26.8 g
Total Nitrogen	1.6 g	3.2 g
Electrolytes, Minerals, Vitamins	Per Individual Patient Requirements	

Children:

Initial total daily dose should be low and increased slowly.
Dosage of NephAmine above 1 g of EAA/kg/day is not recommended.

Fat Emulsion:

Fat emulsion co-administration should be considered when prolonged (more than 5 days) parenteral nutrition is required, in order to prevent essential fatty acid deficiency.

Mixing Instructions:

Parenteral nutrition solutions should be admixed in a laminar flow hood using appropriate aseptic technique.

See Package Insert for full prescribing information.

Rx only

Ordering Information:

Catalog No. S9092-SS, 250 mL bottle, 12 per case

CONTRAINDICATIONS

NephAmine® (Essential Amino Acid Injection) is contraindicated in patients with severe, uncorrected electrolyte and acid-base imbalance, hyperammonemia, decreased (subcritical) circulating blood volume, inborn errors of amino acid metabolism, or hypersensitivity to one or more amino acids present in the solution.

WARNINGS

This product contains sodium bisulfite, a sulfite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in nonasthmatic people.

Safe and effective use of central venous nutrition requires a knowledge of nutrition as well as clinical expertise in recognition and treatment of the complications which can occur. Frequent clinical evaluation and laboratory determinations are necessary for proper monitoring of central venous nutrition. Studies should include blood sugar, serum proteins, kidney and liver function tests, electrolytes, hemogram, carbon dioxide combining power, serum osmolality, blood cultures, blood ammonia levels, and circulating blood volume.

NephAmine does not replace dialysis and conventional supportive therapy in patients with renal failure.

Administration of NephAmine to children, especially in high dose ranges, may result in hyperammonemia.

Administration of NephAmine to neonates and other infants (especially low birth weight infants) may result in elevated plasma amino acid levels (e.g., hypermethionemia) and hyperammonemia. In these very young age groups, amino acid formulations developed specifically for nutritional support of infants and children should be considered.

Clinically significant hypokalemia, hypophosphatemia, or hypomagnesemia may occur as a result of therapy with NephAmine and hypertonic dextrose and replacement therapy may become necessary.

Administration of nitrogen in any form to patients with marked hepatic insufficiency or hepatic coma may result in plasma amino acid imbalances, hyperammonemia, or central nervous system deterioration. NephAmine should, therefore, be used with caution in such patients.

The intravenous administration of these solutions can cause fluid and/or solute overload resulting in dilution of serum electrolyte concentrations, overhydration, congested states or pulmonary edema. The risk of dilutional states is inversely proportional to the solute concentration of the solution infused. The risk of solute overload causing congested states with peripheral and pulmonary edema is directly proportional to the concentration of the solution.

Conservative doses of amino acids should be given, dictated by the nutritional status of the patient.

PRECAUTIONS

General

Clinical evaluation and periodic laboratory determinations are necessary to monitor changes in fluid balance, electrolyte concentrations, and acid-base balance during prolonged parenteral therapy or whenever the condition of the patient warrants such evaluation. Significant deviations from normal concentrations may require the use of additional electrolyte supplements.

In order to promote urea nitrogen reutilization in patients with renal failure, it is essential to provide adequate calories with minimal amounts of the essential amino acids, and to severely restrict the intake of nonessential nitrogen. Hypertonic dextrose solutions are a convenient and metabolically effective source of concentrated calories.

Fluid balance must be carefully monitored in patients with renal failure and care should be taken to avoid circulatory overload, particularly in association with cardiac insufficiency.

In patients with myocardial infarct, infusion of amino acids should always be accompanied by dextrose, since in anoxia, free fatty acids cannot be utilized by the myocardium, and energy must be produced anaerobically from glycogen or glucose.

Strongly hypertonic nutrient solutions should be administered through an indwelling intravenous catheter with the tip located in the superior vena cava.

Special care must be taken when giving hypertonic dextrose to glucose-intolerant patients such as diabetic or prediabetic and uremic patients, especially when the latter are receiving peritoneal dialysis. To prevent severe hyperglycemia in such patients, insulin may be required.

Administration of glucose at a rate exceeding the patient's utilization may lead to hyperglycemia, coma, and death.

Administration of amino acids without carbohydrates may result in the accumulation of ketone bodies in the blood. Correction of this ketonemia may be achieved by the administration of carbohydrates.

Abrupt cessation of hypertonic dextrose infusion may result in rebound hypoglycemia.

When 5.4% NephAmine® (Essential Amino Acid Injection) is subjected to changes in temperature, there is a chance that some transient crystallization of amino acids may occur. Thorough shaking of the bottle for about one minute should redissolve the amino acids. If the amino acids do not completely redissolve, the bottle must be rejected.

To minimize the risk of possible incompatibilities arising from mixing this solution with other additives that may be prescribed, the final infusate should be inspected for cloudiness or precipitation immediately after mixing, prior to administration, and periodically during administration.

Care must be taken to avoid incompatible admixtures. Consult with pharmacist.

Use only if solution is clear and vacuum is present.

Usage in Pregnancy

Pregnancy Category C. Animal reproduction studies have not been conducted with 5.4% NephAmine (Essential Amino Acid Injection). It is also not known whether NephAmine can

cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. NephAmine should be given to a pregnant woman only if clearly needed.

Special Precautions for Central Venous Nutrition

Administration by central venous catheter should be used only by those familiar with this technique and its complications.

Central venous nutrition may be associated with complications which can be prevented or minimized by careful attention to all aspects of the procedure including solution preparation, administration, and patient monitoring. It is essential that a carefully prepared protocol, based on current medical practices, be followed, preferably by an experienced team.

Although a detailed discussion of the complications of central venous nutrition is beyond the scope of this insert, the following summary lists those based on current literature:

Technical. The placement of a central venous catheter should be regarded as a surgical procedure. One should be fully acquainted with various techniques of catheter insertion as well as recognition and treatment of complications. For details of techniques and placement sites, consult the medical literature. X-ray is the best means of verifying catheter placement. Complications known to occur from the placement of central venous catheters are pneumothorax, hemothorax, hydrothorax, artery puncture and transection, injury to the brachial plexus, malposition of the catheter, formation of arterio-venous fistula, phlebitis, thrombosis, and air and catheter embolus.

Septic. The constant risk of sepsis is present during central venous nutrition. Since contaminated solutions and infusion catheters are potential sources of infection, it is imperative that the preparation of parenteral nutrition solutions and the placement and care of catheters be accomplished under controlled aseptic conditions.

Parenteral nutrition solutions should ideally be prepared in the hospital pharmacy under a laminar flow hood. The key factor in their preparation is careful aseptic technique to avoid inadvertent touch contamination during mixing of solutions and subsequent admixtures.

Parenteral nutrition solutions should be used promptly after mixing. Any storage should be under refrigeration for as brief a time as possible. Administration time for a single bottle an set should never exceed 24 hours.

Consult the medical literature for a discussion of the management of sepsis during central venous nutrition. In brief, typical management includes replacing the solution being administered with a fresh container and set, and the remaining contents are cultured for bacterial or fungal contamination. If sepsis persists and another source of infection is not identified, the catheter is removed, the proximal tip cultured, and a new catheter reinserted when the fever has subsided. Nonspecific, prophylactic antibiotic treatment is not recommended. Clinical experience indicates that the catheter is likely to be the prime source of infection as opposed to aseptically prepared and properly stored solutions.

Metabolic. The following metabolic complications have been reported: metabolic acidosis, hypophosphatemia, alkalosis, hyperglycemia and glycosuria, osmotic diuresis and dehydration rebound hypoglycemia, elevated liver enzymes, hypo- and hypervitaminosis, electrolyte imbalances, and elevated plasma amino acid levels and hyperammonemia in infants and children. Frequent clinical evaluation and laboratory determinations are necessary, especial