PRESCRIBING INFORMATION

AMINOSYN@ 8.5% INJECTION WITH ELECTROLYTES

(amino acids for injection 8.5% with electrolytes)

Sulfite-Free

Intravenous Fluid, Nutritive and Electrolytes Supplements

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NAMES OF DRUGS

AMINOSYN® 8.5% Injection with Electrolytes

(amino acids for injection 8.5% with electrolytes)

Sulfite-Free

THERAPEUTIC CLASSIFICATION

Intravenous Fluid, Nutritive and Electrolytes Supplements

ACTION

AMINOSYN® 8.5% Injection with Electrolytes (amino acids for injection 8.5% with electrolytes), Sulfite-Free provides solutions which at a dosage of 1.2 litre/day supply the average daily protein, fluid and electrolytes requirements.

AMINOSYN® 3.5% M Injection
One hundred and six metabolically stable, adult, surgical patients were studied. AMINOSYN® 3.5% M Injection (amino acids for injection 3.5% with maintenance electrolytes) was infused at a dosage of 45 mL/kg/day (1.5 g/kg/day amino acids). No other calorie-containing solutions were given and additional fluid and electrolyte requirements were provided as glucose-free solutions. Patients received infusions for 3-5 days, post-surgically.

While the mean of the clinical parameters examined remained within or close to normal limits, decreased haemoglobin and hematocrit occurred. As well, the mean weight loss was 4 lbs (1.81 kg). Phlebitis and nausea occurred frequently, but did not necessitate stopping the infusion.

INDICATIONS AND CLINICAL USES

Peripheral Vein Administration
AMINOSYN® 8.5% Injection with Electrolytes, a ready-to-use solution, is indicated for peripheral vein infusion as a source of nitrogen in the intravenous treatment of acute adult surgicval patients with adequate sotres of body fat, in whom, for short periods of time (3-5 days), oral nutrition cannot be tolerated or is not desirable. In such instances, the patient's caloric needs are met from their own fat stores. AMINOSYN® 8.5% Injection with Electrolytes must be diluted with sterile water for injection USP before use.

Central Vein Administration
AMINOSYN® 8.5% Injection with Electrolytes when administered with concentrated dextrose solution also is indicated for central vein infusion as an adjunct in the prevention of nitrogen loss or in the treatment of negative nitrogen balance in patients where : (1) the alimentary tract, by the oral, gastronomy or jejunostomy route, cannot or should not be used, (2) gastrointestinal absorption of protein is impaired, or (3) metabolic requirements for protein are substantially increased, as with extensive burns.

CONTRAINDICATIONS

AMINOSYN® 8.5% Injection with Electrolytes are contraindicated in patients with previous hypersensitivity to this product or any of its components.

These preparations should not be used in infants, children or pregnant women. They should not be used in patients with hepatic coma or anuria or metabolic disorders involving impaired nitrogen utilization. Patients with azotemia from any cause should not be infused with amino acids without regard to total nitrogen intake.

WARNINGS

Intravenous infusion of amino acid solutions may induce a rise in blood urea nitrogen (BUN) especially in patients with impaired hepatic or renal function. Appropriate laboratory tests should be performed periodically and infusion discontinued if BUN levels exceed normal post-prandial limits, and continue to rise. It should be noted that a modest rise in BUN normally occurs as a result of increased protein intake.

ADMINISTRATION BY CENTRAL VENOUS CATHETER SHOULD BE USED ONLY BY THOSE FAMILIAR WITH THIS TECHNIQUE AND ITS COMPLICATIONS.

Central vein infusion (with added concentrated carbohydrate solutions) of amino acid solutions 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 during administration (see **PRECAUTIONS – Laboratory Tests**).

Administration of amino acid solutions to a patient with hepatic insufficiency may result in serum amino acid imbalances, metabolic alkalosis, prerenal azotemia, hyperammonemia, stupor and coma.

Hyperammonemia is of special significance in infant as it can result in mental retardation. Therefore, it is essential that blood ammonia levels be measured frequently in infants.

Instances of asymptomatic hyperammonia have been reported in patients without overt liver dysfunction. The mechanisms of this reation are not clearly defined, but may involve genetic defects and immature or subclinically impaired liver function.

Should symptoms of hyperammonia develop, administration should be discontinued and patient's clinical status re-evaluated.

Administration of amino acid solutions in the presence of impaired renal function may augment an increasing BUN, as does any protein dietary component.

Solutions containing sodium ion should be used with great care, if at all, in patients with congestive heart failure, severe renal insufficiency, and in clinical states in which there exists edema with sodium retention.

Solutions which contain potassium ion should be used with great care, if at all, in patients with hyperkalemia, severe renal failure, and in conditions in which potassium retention is present.

Solutions containing acetate ion should be used with great care in patients with metabolic or respiratory alkalosis. Acetate should be administered with great care in those conditions in which there is an increased level or an impaired utilization of this ion, such as severe hepatic insufficiency.

The infusion of hypertonic dextrose may lead to hyperglycemia, glycosuria, and hyperosmolar syndrome, and administration into peripheral vein may result in vein irritation, damage and thrombosis.

Use in Pregnancy

Use in pregnancy has not yet been studied.

Animal reproduction studies have not been conducted with AMINOSYN® with Electrolytes. It is not known whether AMINOSYN® with Electrolytes can cause fetal harm when administered to a pregnant woman. AMINOSYN® with Electrolytes should be given to a pregnant woman only if clearly needed.

PRECAUTIONS

General

In many patients, provision of adequate calories in the form of hypertonic dextrose may require the administration of exogenous insulin to prevent hyperglycemia and glycosuria. To prevent rebound hypoglycemia, a solution containing 5% dextrose should be administered when hypertonic dextrose infusions are abruptly discontinued.

Patients with Special Diseases and Conditions

Special care must be taken when administering dextrose to provide energy in diabetic or prediabetic patients. Frequent blood sugar determinations should govern insulin dosage.

Intravenously administered amino acid solutions should be used with caution in patients with history of renal disease, pulmonary disease, cardiac insufficiency, or with sever congestive heat failure, so as to avoid circulatory overload.

Solutions containing acetate ion should be used with caution, as excess administration may result in metabolic alkalosis.

Nitrogen intake should be carefully monitored in patients with impaired renal function.

Drug Interactions

Additives may be incompatible. When introducing additives, always consult with hospital pharmacist, use aseptic technique, mix thoroughly, and do not store.
Because of its antianabolic activity, concurrent administration of tetracycline may reduce the potential effects of amino acids.

Laboratory Tests

Clinical evaluation and laboratory determinations, at the discretion of the attending physician, are necessary for proper monitoring during administration. Do not withdraw venous blood for blood chemistries through the peripheral infusion site, as interference with estimations of nitrogen containing substances may occur. Blood studies should include glucose, urea nitrogen, serum electrolytes, ammonia, cholesterol, acid-base balance, serum proteins, kidney and liver function tests, osmolarity and hemogram. White blood count and blood cultures are to be determined if indicated. Urinary osmolality and glucose should be determined as necessary.

Serum electrolytes should be monitored and appropriate electrolytes added to the daily infusion regimen. Acid base balance also should be monitored and disturbances in equilibrium corrected, as needed. The amino acid solutions, as formulated, have no potential for increasing hydrogen ion concentrations.

Frequent blood-sugar level measurements should be performed on diabetic patients receiving amino acid solutions.

Use in Children

The effect of infusion of amino acids, without dextrose, upon carbohydrate metabolism of children is not known at this time.

AMINOSYN® WITH ELECTROLYTES MAY NOT BE SUITABLE FOR USE IN YOUNG CHILDREN WHO REQUIRE INDIVIDUALIZED ELECTROLYTE THERAPY.

Long-Term Total Parenteral Nutrition (TPN):

For long-term TPN, or if a patient has inadequate fat stores, it is essential to provide adequate exogenous energy concurrently, if parenterally administered amino acids are to be retained by the body and utilized for protein synthesis.

Concentrated dextrose solutions, with or without fat emulsions, are an effective source of such energy. Strongly hypertonic nutrient solutions (those containing dextrose at a final concentration greater than 10%) should be administered through an indwelling intravenous catheter with the tip located in the superior vena cava.

Special Precautions for Central Venous Infusions

ADMINISTRATION BY CENTRAL VENOUS CATHETER SHOULD BE PERFORMED ONLY BY THOSE FAMILIAR WITH THIS TECHNIQUE AND ITS COMPLICATIONS.

Central vein infusion of amino acid solutions (with added concentrated carbohydrate solutions) requires a knowledge of nutrition as well as clinical expertise in recognition and treatment of complications which can occur. Complications can be prevented or minimized by paying careful attention to 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 is beyond the scope of this monograph, the following summary lists those based on current literature:

1. 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 arteriovenous fistula, phlebitis, thrombosis and air and catheter emboli.

2. Septic:

The constant risk of sepsis, especially fungal septicemia, is present during administration of all parenteral nutritional solutions. Since contaminated solutions and infusion catheters are potential sources of infection, it is imperative that the preparation of the solution and the placement and care of catheters be accomplished under controlled aseptic conditions.

Ideally, solutions should be prepared in the hospital pharmacy under a laminar-flow hood using careful aseptic techinique to avoid inadvertent touch containiation during mixing of solutions and addition of other nutrients. Solutions should be used promptly after mixing. Any storage should be under refrigeration and limited to a brief period of time less than 24 hours.

Administration time for a single container and set should never exceed 24 hours.

Do not administer any parenteral nutrition as a 3 in 1 mixture if the emulsion is cracked and/or oil is visible at the surface of the parenteral nutrition.

The typical management of sepsis includes replacing the solution being administered with a fresh container and set, and culturing the remaining solution for bacterial or fungal contamination. If sepsis persists and another source of infection is not identified, the catheter is removed, proximal tip cultured and a new catheter inserted when the fever has subsided. Non-specific prophylactic 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.

3. Metabolic:
The following complications have been reported: metabolic acidosis and alkalosis, hypophosphatemia, hypocalcemia, osteoporosis, hyperglycemia and glycosuria, hyperosmotic nonketotic states and dehydration, osmotic diuresis and dehydration, rebound hypoglycemia, elevated liver enzymes, hypo- and hyper-vitaminosis, electrolyte imbalances and hyperammonemia in children. Frequent clinical evaluation and laboratory determinations are necessary, especially during the first few days of therapy, to prevent or minimize these complications.

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

ADVERSE REACTIONS

Hypersensitivity reactions ranging from rash and fever to hives, respiratory difficulties and anaphylaxis have been noted. Local injection site reactions have also been noted.

Generalized flushing, fever and nausea have been reported during infusions of amino acid solutions.

See **WARNINGS** and **Special Precautions for Central Infusions**.

Peripheral Infusions

Local reactions consisting of a warm sensation, erythema, phlebitis, and thrombosis at the infusion site have been reported with peripheral intravenous infusion of amino acids particularly if other substances, such as antibiotics are also administered through the same site. In such cases, the infusion site should be changed promptly to another vein. Use of large peripheral veins and slowing the rate of infusion may be helpful in decreasing the incidence of local venous irritation. Electrolyte additives should be spread throughout the day. Irritating additive medications may need to be injected at another venous site and should not be added to the amino acid solution.

SYMPTOMS AND TREATMENT OF OVERDOSAGE

In the event of overhydration or solute overload, re-evaluate the patient and institute appropriate corrective measures (see **WARNINGS** and **PRECAUTIONS**).

Potential overdosage with amino acid solutions will be indicated by nausea, chills, tachycardia, abdominal pain and flushing. Should such symptoms persist, the administration of the solution should be terminated and the patient observed for remission of these complaints. Plasma electrolyte determinations will indicate if a state of water intoxication exists and what treatment should be instituted to correct this condition. Normally, when the dosage prescribed is administered as directed, overdosage will not occur.

DOSAGE AND ADMINISTRATION

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

Additives may be incompatible. When introducing additives, always consult with hospital pharmacist, use aseptic technique, mix thoroughly, and do not store.

The total daily dose of amino acid solution depends on daily protein requirements and the patient's metabolic and clinical response.

As with all intravenous therapy, the primary aim is to provide sufficient water to compensate for insensible, urinary and other (nasogastric suction, fistula drainage, diarrhea) fluid losses. Those requirements as well as electrolyte and acid/base needs should be estimated and appropriately prescribed.

Given an amino acid solution of specified total concentration, the volume needed to meet amino acid requirements per 24 hours can be calculated. After making an estimate of the total daily fluid (water) requirement, the balance of fluid needed beyond the volume of amino acid solution required can be provided as a noncarbohydrate- or carbohydrate-containing electrolyte solution.

Peripheral Vein Administration:

AMINOSYN® 8.5% Injection with Electrolytes must be diluted with sterile water for injection USP prior to administration so that a total dose of 1.5 g/kg/day of amino acids is not exceeded. AMINOSYN® 8.5% Injection with Electrolytes should not be infused via a central vein unless admixed with sufficient dextrose to provide full caloric energy requirements in patients who require prolonged total parenteral nutrition. When amino acids (without dextrose) are infused peripherally, care should be taken to avoid oral ingestion of carbohydrate or infusion of carbohydrate-containing solutions if fat mobilization is desired as the source of energy. Otherwise, full mobilization may not occur.

For peripheral vein infusion, 1 to 1.5 g/kg/day of total amino acids will achieve optimal fat mobilization and spare protein catabolism. No carbohydrate should be infused or ingested.

A patient given the recommended maintenance fluid requirement of 45 mL/kg/day in the form of AMINOSYN® 8.5% Injection with Electrolytes (amino acids for injection 8.5% with electrolytes) diluted with water will receive the average daily requirements for sodium, potassium, magnesium, and chloride along with an optimal amount of amino acids for preservation of nitrogen balance.

If desired, one-half of an estimated daily amino acid requirement of 1.5 g/kg can be given on the first day. The degree of fat mobilization can be gauged by the presence and amount of acetonuria. Amino acid dosage may be increased on the second day. Amino acid infusion into a peripheral vein can be continued as long as oral nutrition is impaired. However, if a patient is unable to take oral nourishment at the end of 5 days, institution of total parenteral nutrition with exogenous calories should be considered.

Central Vein Administration:

Adjunctive for total parenteral nutrition. AMINOSYN® 8.5% Injection with Electrolytes can be administered by the central intravenous route with a concentrated dextrose solution. The determination of nitrogen balance and accurate daily body weights, corrected for fluid balance, are probably the best means of assessing individual protein requirements. For patients in a stable metabolic condition, the provision of amino acids as a 3.5% concentration with 20 to 25% dextrose is usually considered adequate.

AMINOSYN® 8.5% Injection with Electrolytes (500 mL) may be diluted with 500 mL of dextrose 50% Injection to give a solution of 4.25% amino acids and 25% dextrose. This solution, with a higher concentration of nitrogen and calories per unit volume, is indicated for patients requiring larger amounts of nitrogen than could otherwise be provided, or where the total fluid load must be kepy to a minimum.

SERUM ELECTROLYTES SHOULD BE MONITORED AS INDICATED. Electrolytes may be added to the nutrient solution as indicated by patient's clinical condition and laboratory determinations of plasma values. Major electrolytes are sodium, chloride, potassium, phosphate, and magnesium. All these electrolytes are included in AMINOSYN® with Electrolytes. Vitamins, including folic acid and vitamin K are required additives. The trace element supplements should be given when long-term TPN is undertaken.

Potentially incompatible ions, such as calcium and phosphate, may be added to alternate infusate bottles to avoid precipitation. If one additive is added to the amino acid container, and the other to the container of concentrated dextrose, and if the contents of both containers are swirled before they are combined, then the likelihood of physical incompatibility is reduced.

If the rate of administration should fall behind schedule, no attempt to "catch up" to planned intake should be made.

To prevent rebound hypoglycemia, do not discontinue administration of solution abruptly.

Iron is added to the solution or given intramuscularly in depot form as indicated. Vitamin B_{12}, vitamin K and folic acid are given intramuscularly or added to the solution as desired.

In patients with hyperchloremic or other metabolic acidosis, sodium and potassium may be added as the acetate or lactate salts to provide bicarbonate alternates.

Provisions of adequate energy in the form of hypertonic dextrose may require exogenous insulin to prevent hyperglycemia and glycosuria. Ensure that exogenous insulin activity has ceased, before abruptly discontinuing nutrient solution.

AVAILABILITY

AMINOSYN® 8.5% Injection with Electrolytes (amino acids for injection 8.5% with electrolytes) is supplied in 500 and 1000 mL - PVC bags.

Each litre of AMINOSYN® 8.5% Injection with Electrolytes provides a total equivalent of 85 g of protein and 13.4 g of nitrogen.

PHARMACOLOGY

AMINOSYN® 8.5% Injection with Electrolytes (amino acids for injection 8.5% with electrolytes) are sterile, non-pyrogenic solutions for peripheral intravenous infusion.

AMINOSYN® 8.5% Injection with Electrolytes is also indicated for central vein infusion when administered with concentrated dextrose solution.

All of the amino acids are present in the metabolizable L-form and the acetate salt of Lysine is used instead of the hydrochloride salt in order to reduce the potential for precipitating or exacerbating metabolic acidosis during infusion of the solution.

The solution also contains maintenance doses of the principal electrolytes. A patient receiving the adult average daily fluid requirement of 1.2 litres as AMINOSYN® 8.5% Injection with Electrolytes (amino acids for injection 8.5% with electrolytes), will receive electrolytes in amounts that meet the minimum daily requirements of the average adult. At the same time, the patient receives a total of 102-104 g amino acids, the optimal amount for preservation of nitrogen balance in a metabolically stable 70 kg adult.

AMINOSYN® 8.5% Injection with Electrolytes (amino acids for injection 8.5% with electrolytes) provides the following quantities of amino acids and electrolytes expressed as mg / 100 mL solution.

Essential Amino Acids (mg/100 mL)	
Isoleucine	620
Leucine	810
Lysine (acetate)*	624
Methionine	340
Phenylalanine	380
Threonine	460
Tryptophan	150
Valine	680

*Amount cited is for lysine alone and does not include the acetate salt.

Nonessential Amino Acids (mg/100 mL)	
Alanine	1100
Arginine	850
Histidine	260
Proline	750
Serine	370
Tyrosine	44
Glycine	1100

Product Characteristics	
Osmolarity (mOsmol/L)	1040
pH	5.2

Electrolytes		
	mmol/L	mEq/L
Sodium	65	65
Potassium	65	65
Magnesium	5	10
Phosphate	30	60
Chloride	98	98
Acetate	142	142

Electrolytes (mg/100 mL)	
Sodium Chloride	28
Magnesium Chloride hexahydrate	102
Sodium Phosphate, dibasic	425
Potassium Chloride	487

Storage Conditions

Store between 20° and 25°C. Do not freeze. Protect from light. Avoid excessive heat.

These solutions contain no bacteriostat. Any unused remainder should be discarded.

Stability and Storage Recommendations following Constitution

Solutions should be used promptly after mixing. Any storage should be under refrigeration and limited to a brief period of time less than 24 hours.

Administration time for a single container and set should never exceed 24 hours.