

## **PRESCRIBING INFORMATION**

**AMINOSYN™**

(amino acids for injection 10%)

**Sulfite-Free**

**Nutritive Supplement for Intravenous Infusion**

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Control No. 210260

**NAME OF DRUG:**

AMINOSYN™

(amino acids for injection 10%)

Sulfite-Free

**THERAPEUTIC OR PHARMACOLOGICAL CLASSIFICATION**

Nutritive Supplement for Intravenous Infusion

**ACTION**

1. **Protein Sparing (Peripheral Use):**

It has been shown that it may be preferable for short periods of time, 3 to 5 days, to mobilize fat (as in total starvation) for meeting energy requirements to spare protein.

Under conditions of total fasting, lipid mobilization provides energy substrate in the form of free fatty acids and ketone bodies. Lipolysis occurs because insulin levels are low. If high concentrations of carbohydrates are administered, insulin levels will rise and inhibit lipid mobilization. With brief periods of fasting (less than 24 hours), energy requirements are usually met by glycogenolysis of the glycogen stored in the liver. However, after glycogen is depleted, lipolysis of body fat becomes the fat source of energy.

Thus, when amino acids (without dextrose) are infused into a peripheral vein, lipolysis and ketogenesis occur freely and caloric requirements are met without proteolysis. This spares protein and the body's muscle mass, while providing a substrate for essential protein synthesis.

Amino acid peripheral intravenous infusions result in: (1) availability of free fatty acids and ketone bodies as sources of energy, and (2) the concomitant utilization of administered amino acids for protein synthesis.

2. **Adjunctive For Total Parenteral Nutrition (TPN):**

Central vein infusion should be considered when amino acid solutions are to be admixed with sufficient dextrose to meet fully caloric energy requirements for protein synthesis in patients requiring prolonged total parenteral nutrition. Because of the highly irritant effect of hypertonic dextrose solutions required to meet total energy needs over prolonged periods, peripheral vein infusion of such solutions is not feasible. However, amino acids, infused together with total calories provided by concentrated dextrose into a central vein, are utilized for repair and maintenance of body proteins.

## **INDICATIONS AND CLINICAL USES**

### **Peripheral Vein Administration**

Aminosyn (amino acids for injection 10%) is indicated for peripheral vein infusion as a source of nitrogen in the intravenous treatment of acute surgical patients.

In those patients with adequate stores of body fat, for short periods of time oral nutrition cannot be tolerated or is not desirable. In such instances, the patients' caloric needs are met from their own fat stores.

### **Central Vein Administration**

Amino acids, when administered with concentrated dextrose solutions are also 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, gastrostomy 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 or in renal failure patients who cannot eat.

AMINOSYN, when administered with Dextrose 50% Injection, is designed for central vein infusion only. It is intended to meet the needs of hypermetabolic patients, such as those with burns or trauma. It permits administration of great amounts of nitrogen and calories without excessive fluid. This latter consideration is of importance in patients with cardiac or renal disease.

## **CONTRAINDICATIONS**

AMINOSYN is contraindicated in patients with previous hypersensitivity to this product or any of its components.

This preparation 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 postprandial 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.

THIS PRODUCT CONTAINS ALUMINUM THAT MAY BE TOXIC. ALUMINUM MAY REACH TOXIC LEVELS WITH PROLONGED PARENTERAL ADMINISTRATION IF KIDNEY FUNCTION IS IMPAIRED. PREMATURE NEONATES ARE PARTICULARLY AT RISK BECAUSE THEIR KIDNEYS ARE IMMATURE, AND THEY REQUIRE LARGE AMOUNTS OF CALCIUM AND PHOSPHATE SOLUTIONS, WHICH CONTAIN ALUMINUM.

RESEARCH INDICATES THAT PATIENTS WITH IMPAIRED KIDNEY FUNCTION, INCLUDING PREMATURE NEONATES, WHO RECEIVE PARENTERAL LEVELS OF ALUMINUM AT GREATER THAN 4 TO 5  $\mu\text{G}/\text{KG}/\text{DAY}$  ACCUMULATE ALUMINUM AT LEVELS ASSOCIATED WITH CENTRAL NERVOUS SYSTEM AND BONE TOXICITY. TISSUE LOADING MAY OCCUR AT EVEN

## LOWER RATES OF ADMINISTRATION.

**Central Vein Administration:** Central vein infusion (with added concentrated carbohydrate solutions) of amino acid solutions requires 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 infants, as it can result in mental retardation. It is essential that blood ammonia be measured frequently in infants.

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

Should symptoms of hyperammonemia 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.

### **Use in Neonates:**

The safety and efficacy of AMINOSYN in neonates has not been demonstrated.

### **Use in Children:**

The effect of infusion of amino acid solutions, without dextrose, upon carbohydrate metabolism of children is not known at this time. Therefore, such usage of amino acids for injection 10% in children is not recommended.

### **Use in Pregnancy:**

Use in pregnancy has not yet been studied. Animal reproduction studies have not been conducted with AMINOSYN. It is not known whether AMINOSYN can cause fetal harm when administered to a pregnant woman. AMINOSYN 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 giving hypertonic glucose to diabetic or pre-diabetic patients. Frequent blood sugar determinations should govern insulin dosage.

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

Intravenously administered amino acids solutions should be used with caution in patients with history of renal disease, pulmonary disease, cardiac insufficiency or with severe congestive heart failure, so as to avoid excessive fluid replacement.

## **Drug Interactions**

Because of its antianabolic activity, concurrent administration of tetracycline may reduce the potential effects of amino acids infused with dextrose as part of a parenteral feeding regimen.

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

## **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.

Because AMINOSYN is strongly hypertonic, they should not be given by peripheral vein unless they can be diluted to form a solution which is isotonic. All additives, such as trace elements, etc., should be taken into account for the dilution.

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.

Do not withdraw venous blood for blood chemistries through the peripheral infusion site; as interference with estimations of nitrogen-containing substances may occur.

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

## **Long-Term Total Parenteral Nutrition:**

For long-term total nutrition, or if a patient has inadequate fat stores, it is essential to provide adequate

exogenous calories concurrently, if parenterally administered amino acids are to be retained by the body and utilized for protein synthesis. Concentrated dextrose solutions are an effective source of such calories.

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

### **SPECIAL PRECAUTIONS FOR CENTRAL INFUSIONS**

Administration of amino acid solutions with concentrated dextrose and other nutrients via central venous catheter may be associated with complications which can be prevented or minimized by 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 embolus.

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. The key factor in their preparation is careful aseptic technique to avoid inadvertent touch contamination 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.

3. **Metabolic:**

The following complications have been reported with TPN administration: metabolic acidosis, hypophosphatemia, alkalosis, hypocalcemia, osteoporosis, hyperglycemia and glycosuria, 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.

This product contains no more than 25 µg/L of aluminum.

### **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, inline filters, 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, and irritating additive medications may need to be injected at another venous site.

## **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. Normally, when the dosage prescribed is administered as directed, overdosage will not occur. 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.

## **DOSAGE AND ADMINISTRATION**

DO NOT USE FLEXIBLE CONTAINER IN SERIES CONNECTIONS.

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:**

### **Protein sparing:**

AMINOSYN (without dextrose) can be administered by the peripheral intravenous route.

AMINOSYN must be diluted prior to administration, so that a total dose of 1.5 g/kg/day of amino acids is not exceeded. AMINOSYN 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.

Vitamins and additional electrolytes as needed to correct imbalances may be added to the amino acid solution. Solutions of bicarbonate may be added to amino acid solutions, but the order of addition is important if precipitation problems are to be avoided. 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:**

For central vein infusion with concentrated dextrose solution, the total daily dose of amino acid solution depends on daily protein requirements and the patient's metabolic and clinical response. 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. Vitamins, minerals and electrolytes should be added as indicated.

AMINOSYN can be diluted with an equal volume of Dextrose 50% Injection to give solutions containing 5% amino acids, respectively, and 25% dextrose. These solutions, with a higher concentration of nitrogen and calories per unit volume, are indicated for patients requiring larger amounts of nitrogen than could otherwise be provided, or where the total fluid load must be kept to a minimum.

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.

Potentially incompatible ions, such as calcium and phosphate, may be added to alternate infusate containers 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.

AMINOSYN SOLUTIONS WITHOUT ELECTROLYTES ARE INTENDED FOR PATIENTS REQUIRING INDIVIDUALIZED ELECTROLYTES THERAPY. SERUM ELECTROLYTES SHOULD BE MONITORED AS INDICATED. Electrolytes may be added to the nutrient solution as indicated by the patient's clinical condition and laboratory determinations of plasma values. Major electrolytes are sodium, chloride, potassium, phosphate, magnesium and calcium. Vitamins, including folic acid and vitamin K are required additives. The trace element supplements should be given when long-term TPN is undertaken.

Iron is added to the solution or given intramuscularly in depot form as indicated. Vitamin B<sub>12</sub>, 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.

In adults, hypertonic mixtures of amino acids and dextrose may be safely administered by continuous infusion through a central venous catheter with the tip located in the superior vena cava.

### **AVAILABILITY**

AMINOSYN is supplied in 500 mL and 1000 mL flexible plastic containers.

A 500 mL or 1000 mL unit of AMINOSYN provides a total equivalent of 100 g/L of protein and 15.72 g/L of nitrogen. The pH (range) is 5.2 (4.5 to 6.0) adjusted with acetic acid. The osmolarity is 932 mOsmol/L. Approx. mmol or mEq/L: acetate 147.

### **Storage Conditions:**

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

The flexible plastic container is fabricated from a specially formulated polyvinylchloride. Water can permeate from inside the container into the overwrap but not in amounts sufficient to affect the solution significantly.

Solutions in contact with the plastic container may leach out certain chemical components from the plastic in very small amounts; however, biological testing was supportive of the safety of the plastic container materials.

Exposure to temperature above 25 °C/77°F during transport and storage will lead to minor losses in moisture content. Higher temperatures lead to greater losses. It is unlikely that these minor losses will lead to clinically significant changes within the expiration period.

### **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.

## CHEMISTRY

AMINOSYN (amino acids for injection 10%) is a sterile, non-pyrogenic solution for intravenous infusion. Aminosyn is oxygen sensitive.

All 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 following formula represents the optimal proportions of component crystalline amino acids in AMINOSYN expressed in grams (g) per 100 grams of amino acid content.

In the case of the amino acid L-Tyrosine, whose solubility is 0.44 mg/mL at room temperature (20°C), the amount present in the optimal formulation does not vary with the concentration of other amino acids and thus the actual amount of this amino acid in AMINOSYN will remain constant.

### ESSENTIAL AMINO ACIDS

L-Isoleucine	7.3
L-Leucine	9.5
L-Lysine (as acetate)	7.3
L-Methionine	4.0
L-Phenylalanine	4.5
L-Threonine	5.2
L-Tryptophan	1.6
L-Valine	8.1

### NON-ESSENTIAL AMINO ACIDS

L-Alanine	12.9
L-Arginine	9.9
L-Histidine	3.0
L-Proline	8.7
L-Serine	4.2
L-Tyrosine	0.9
Glycine (Aminoacetic acid)	12.9

AMINOSYN solution provides the following quantities of amino acids.

**Aminosyn Formulation**  
**Essential Amino Acids (mg/100 mL)**

<b>Aminosyn</b>	<b>10%</b>
Isoleucine	720
Leucine	940
Lysine (acetate)*	720
Methionine	400
Phenylalanine	440
Threonine	520
Tryptophan	160
Valine	800

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

**Nonessential Amino Acids (mg/100 mL)**

<b>Aminosyn</b>	<b>10%</b>
Alanine	1280
Arginine	980
Histidine	300
Proline	860
Serine	420
Tyrosine	44
Glycine	1280

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