74-8027-7
(Rev July 2004)

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Baxter

Novamine® 15%
Amino Acids Injection

Pharmacy Bulk Package
Not For Direct Infusion

DESCRIPTION

Novamine® 15% Amino Acids Injection in a Pharmacy Bulk Package is a sterile, clear, nonpyrogenic solution of essential and nonessential amino acids for intravenous infusion in parenteral nutrition following appropriate dilution. Novamine® 15% in a Pharmacy Bulk Package is not for direct infusion. It is a sterile dosage from which contains several single doses for use in a pharmacy admixture program in the preparation of intravenous parenteral fluids.

Each 100 mL contains:

Essential Amino Acids		
Lysine (from Lysine Acetate, USP)	1.18	g
Leucine, USP	1.04	g
Phenylalanine, USP	1.04	g
Valine, USP	960	mg
Isoleucine, USP	749	mg
Methionine, USP	749	mg
Threonine, USP	749	mg
Tryptophan, USP	250	mg
Nonessential Amino Acids		
Alanine, USP	2.17	g
Arginine, USP	1.47	g
Glycine, USP	1.04	g
Histidine, USP	894	mg
Proline, USP	894	mg
Glutamic Acid	749	mg
Serine, USP	592	mg
Aspartic Acid, USP	434	mg
Tyrosine, USP	39	mg
Sodium Metabisulfite, NF added	30	mg
Water for Injection, USP		qs
Essential Amino Acids	6.7	g
Nonessential Amino Acids	8.3	g
Total Amino Acids	15.0	g
Total Nitrogen	2.37	g
Acetate*	151	mEq/L
Osmolarity (calculated)	1388	mOsmol/L
pH	5.6 (5.2-6.0)	

*Acetate from Lysine Acetate, USP and acetic acid used for pH adjustment.

The formulas for the Individual amino acids are as follows:

Essential Amino Acids

Lysine Acetate: $H_2N(CH_2)_4CH(NH_2)COOH{\cdot}CH_3COOH$

Leucine: $(CH_3)_2CHCH_2CH(NH_2)COOH$

Phenylalanine:

$CH_2CH(NH_2)COOH$

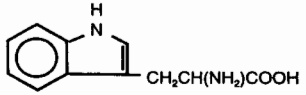
Valine: $(CH_3)_2CHCH(NH_2)COOH$

Isoleucine: $CH_3CH_2CH(CH_3)CH(NH_2)COOH$

Methionine: $CH_3S(CH_2)_2CH(NH_2)COOH$

Threonine: $CH_3CH(OH)CH(NH_2)COOH$

Tryptophan:



$CH_2CH(NH_2)COOH$

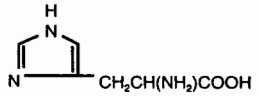
Nonessential Amino Acids

Alanine: $CH_3CH(NH_2)COOH$

Arginine: $H_2NC(NH)NH(CH_2)_3CH(NH_2)COOH$

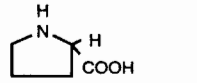
Glycine: H_2NCH_2COOH

Histidine:



$CH_2CH(NH_2)COOH$

Proline:

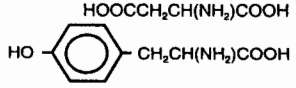


Glutamic Acid: $HOOC(CH_2)_2CH(NH_2)COOH$

Serine: $HOCH_2CH(NH_2)COOH$

Aspartic Acid: $HOOCCH_2CH(NH_2)COOH$

Tyrosine:



$CH_2CH(NH_2)COOH$

CLINICAL PHARMACOLOGY

Novamine® 15% Amino Acids Injection provides seventeen crystalline amino acids. This completely utilizable substrate promotes protein synthesis and wound healing and reduces the rate of protein catabolism.

A. Total Parenteral Nutrition (Central Infusion)

When enteral feeding is inadvisable, Novamine® 15% given by central venous infusion in combination with energy sources, vitamins, trace elements and electrolytes, will completely satisfy the requirements for weight maintenance or weight gain, depending upon the dose selected. The energy component in parenteral nutrition by central infusion may be derived solely from dextrose or may be provided by a combination of dextrose and intravenous fat emulsion. The addition of intravenous fat emulsion provides essential fatty acids and permits a dietary balance of fat and carbohydrate, at the same time offering the option of reducing the dextrose load and/or increasing the total caloric input. An adequate energy supply is essential for optimal utilization of amino acids.

B. Total Parenteral Nutrition (Peripheral Infusion)

Novamine® 15% can also be administered as part of a total parenteral nutrition program by peripheral vein when the enteral route is inadvisable and use of the central venous catheter is contraindicated.

Reduction of protein loss can be achieved by use of diluted Novamine® 15% in combination with dextrose or with dextrose and intravenous fat emulsion by peripheral infusion. Complete peripheral intravenous nutrition can be achieved in patients with low caloric requirements by a Novamine® 15%-dextrose-fat regimen.

INDICATIONS AND USAGE

Novamine® 15% is indicated as an amino acid (nitrogen) sour nutrition regimens. This use is appropriate when the enteral rout inadequate or not possible, as when:

— Gastrointestinal absorption is impaired by obstruction, inflam its complications, or antineoplastic therapy;
— Bowel rest is needed because of gastrointestinal surgery or i such as ileus, fistulae or anastomotic leaks;
— Tube feeding methods alone cannot provide adequate nutriti

CONTRAINDICATIONS

This solution should not be used in patients in hepatic coma, s failure, metabolic disorders involving impaired nitrogen utilization ty to one or more amino acids.

WARNINGS

Administration of amino acids solutions at excessive rates or t hepatic insufficiency may result in plasma amino acid imbalance mia, prerenal azotemia, stupor and coma. Conservative doses o should be given to these patients, dictated by the nutritional statu Should symptoms of hyperammonemia develop, amino acid adm be discontinued and the patient's clinical status re-evaluated.

Contains sodium metabisulfite, a sulfite that may cause allergi including anaphylactic symptoms and life-threatening or less seve episodes in certain susceptible people. The overall prevalence o in the general population is unknown and probably low. Sulfite se more frequently in asthmatic than in nonasthmatic people.

WARNING: This product contains aluminum that may be toxic. A reach toxic levels with prolonged parenteral administration if kidr impaired. Premature neonates are particularly at risk because th immature, and they require large amounts of calcium and phospl which contain aluminum.

Research indicates that patients with impaired kidney function mature neonates, who receive parenteral levels of aluminum at g µg/kg/day accumulate aluminum at levels associated with centra and bone toxicity. Tissue loading may occur at even lower rates

PRECAUTIONS

A. GENERAL

It is essential to provide adequate calories concurrently if par tered amino acids are to be retained by the body and utilized thesis.

The administration of Novamine® 15% Amino Acids Injection parenteral nutrition (TPN) with large volumes of hyperosmoti periodic monitoring of the patient for signs of hyperosmolarity glycosuria and hypertriglyceridemia.

During parenteral nutrition with concentrated dextrose and a tions, essential fatty acid deficiency syndrome may develop clinically apparent. Early demonstration of this condition can plished by gas liquid chromatographic analysis of plasma lipi may be prevented or corrected by appropriate treatment with emulsions.

For complete nutritional support, TPN regimens must also in vitamins and trace elements. Potentially incompatible ions su phosphate may be added to alternate infusate bottles to avoi Although the metabolizable acetate ion in Novamine® 15% di of acidosis, the physician must be alert to the potential appe order.

Initiation and termination of infusions of TPN fluids must be g adjustment of endogenous insulin release.

Undiluted Novamine® 15% should not be administered perip administered centrally, it should be diluted with appropriate d trose, electrolytes and other nutrient components, to at least DOSAGE AND ADMINISTRATION.

Caution against volume overload should be exercised.

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

B. Laboratory Tests

Infusion of Novamine® 15% without concomitant infusion of an adequate number of non-protein calories may result in elevated BUN. Monitoring of BUN is required and the balance between Novamine® 15% and the calorie source may require adjustment. Frequent clinical evaluations and laboratory determinations are required to prevent the complications which may occur during the administration of solutions used in TPN. Laboratory tests should include blood glucose, serum electrolytes, liver and kidney function, serum osmolarity, blood ammonia, serum protein, pH, hematocrit, WBC and urinary glucose. When Novamine® 15% is combined with electrolytes, care should be used in administering this solution to patients with congestive heart failure, renal failure, edema, adrenal hyperactivity, acid-base imbalance and those receiving diuretics or antihypertensive therapy. Total volume infused should be closely monitored. Serum electrolytes should be monitored daily in these patients.

C. Carcinogenesis, Mutagenesis, Impairment of Fertility

Studies with Novamine® 15% have not been performed to evaluate carcinogenic potential, mutagenic potential, or effects on fertility.

D. Pregnancy Category C

Animal reproduction studies have not been conducted with Novamine® 15%. It is also not known whether Novamine® 15% can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Novamine® 15% should be given to a pregnant woman only if clearly needed.

E. Nursing Mothers

Caution should be exercised when Novamine® 15% is administered to a nursing woman.

F. Pediatric Use

Safety and effectiveness of Novamine® 15% Amino Acids Injection in pediatric patients have not been established by adequate and well-controlled studies. However, the use of amino acids injections in pediatric patients as an adjunct in the offsetting of nitrogen loss or in the treatment of negative nitrogen balance is referenced in the medical literature.

G. Special Precautions for Central Infusion

TPN delivered by indwelling catheter through a central or large peripheral vein is a special technique requiring a team effort by physician, nurse and pharmacist. The responsibility for administering this therapy should be confined to those trained in the procedures and alert to signs of complications. Complications known to occur from the placement of central venous catheter 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/catheter emboli. The risk of sepsis is present during intravenous therapy, especially when using central venous catheters for prolonged periods. It is imperative that the preparation of admixtures and the placement and care of the catheters be accomplished under controlled aseptic conditions.

H. Admixtures

Admixtures should be prepared under a laminar flow hood using aseptic technique.

Admixtures should be stored under refrigeration and must be administered within 24 hours after removal from refrigerator.

Filters of less than 1.2 micron pore size must not be used with admixtures containing fat emulsion.

I. Do not administer unless solution is clear and the seal is intact.

IT IS ESSENTIAL THAT A CAREFULLY PREPARED PROTOCOL, BASED ON CURRENT MEDICAL PRACTICES, BE FOLLOWED, PREFERABLY BY AN EXPERIENCED TEAM.

ADVERSE REACTIONS

See WARNINGS, PRECAUTIONS and Special Precautions for Central Infusion.

OVERDOSAGE

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

DOSAGE AND ADMINISTRATION

The appropriate daily dose of amino acids to be used with dextrose or with dextrose and intravenous fat emulsion will depend upon the metabolic status and clinical response of the patient as therapy proceeds. Doses which achieve nitrogen equilibrium or positive balance are the most desirable. The dosage on the first day should be approximately half the anticipated optimal dosage and should be increased gradually to minimize glycosuria; similarly, withdrawal should be accomplished gradually to avoid rebound hypoglycemia.

Fat emulsion coadministration should be considered when prolonged (more than 5 days) parenteral nutrition is required in order to prevent essential fatty acid deficiency (EFAD). Serum lipids should be monitored for evidence of EFAD in patients maintained on fat free TPN.

The amount administered is dosed on the basis of amino acids/kg of body weight/day. In general, two to three g/kg of body weight for neonates and infants with adequate calories are sufficient to satisfy protein needs and promote positive nitrogen balance. In pediatric patients, the final solution should not exceed twice normal serum osmolarity (718 mOsmol/L).

DIRECTIONS FOR PROPER USE OF PHARMACY BULK PACKAGE

Novamine® 15% in a Pharmacy Bulk Package is not intended for direct infusion. The container closure may be penetrated only once using a suitable sterile transfer device or dispensing set which allows measured dispensing of the contents. The Pharmacy Bulk Package is to be used only in a suitable work area such as a laminar flow hood (or an equivalent clean air compounding area). Once the closure is penetrated, the contents should be dispensed as soon as possible; the transfer of contents must be completed within 4 hours of closure entry. The bottle may be stored at room temperature (25°C) after the closure has been entered. Date and time of container entry should be noted in the area designated on the container label.

When using Novamine® 15% in patients with a need for fluid volume restriction, it can be diluted as follows:

	Volume	Amount	Final Concentration
Novamine® 15%	500 mL	75 g	7.5%
Dextrose 70%	250 mL	175 g	17.5%
Intralipid® 20%	250 mL	50 g	5.0%

This will provide 1395 kilocalories (kcal) per 1000 mL of admixture with a ratio of 118 non-protein calories per gram of nitrogen and an osmolarity of 1561 mOsmol/L.

In patients where the need for fluid restriction is not so marked, either of the following regimens may be used dependent upon the energy needs of the patient.

	Volume	Amount	Final Concentration
Novamine® 15%	500 mL	75 g	3.75%
Dextrose 50%	1000 mL	500 g	25%
Intralipid® 20%	500 mL	100 g	5%

This will provide 1500 kcal per 1000 mL of admixture with a ratio of 228 non-protein calories per gram of nitrogen and an osmolarity of 1633 mOsmol/L.

Novamine® 15%	500 mL	75 g	3.75%
Dextrose 30%	1000 mL	300 g	15%
Intralipid® 10%	500 mL	50 g	2.5%

This will provide 935 kcal per 1000 mL of admixture with a ratio of 158 non-protein calories per gram of nitrogen and an osmolarity of 1128.5 mOsmol/L.

A. Total Parenteral Nutrition (Central Infusion)

In unstressed adult patients with no unusual nitrogen losses, a minimum dosage of 0.1 gram nitrogen (4.2 mL of Novamine® 15%) plus 4.4 grams (15 calories) of dextrose per kilogram of body weight per day are required to achieve nitrogen balance and weight stability. Intravenous fat emulsion may be used as a partial substitute for dextrose. This regimen provides a ratio of 150 non-protein calories per gram of nitrogen.

For patients stressed by surgery, trauma or sepsis, and those with unusual nitrogen losses, the dosage required for maintenance may be as high as 0.3 to 0.4 grams of nitrogen (13 to 17 mL Novamine® 15%) per kilogram of body weight per day, with proportionate increases in non-protein calories. Periodic assessment of nitrogen balance of the individual patient is the proper dosage. Volume overload and glycosuria may be enco dosage, and nitrogen balance may not be achieved in extrem bolic patients under these constraints. Concomitant insulin ad be required to minimize glycosuria. Daily laboratory monitorin

Use of an infusion pump is advisable to maintain a steady infu central venous infusion.

B. Peripheral Nutrition

In patients for whom central venous catheterization is not advi catabolism can be reduced by peripheral use of diluted Novan non-protein calorie sources. Dilution of 250 mL Novamine® 15 10% dextrose will reduce the osmolarity to a level (724 mOsm more favorable to the maintenance of the integrity of the walls Intravenous fat emulsion can be infused separately or simultar infused simultaneously the fat emulsion will provide a dilution osmolarity while increasing the energy supply.

Parenteral drug products should be inspected visually for particula discoloration prior to administration, whenever solution and contai

To reduce the risk of bacterial contamination, all intravenous admi should be replaced at least every 24 hours. Usage of admixtures r within 24 hours after mixing. If storage is necessary during this 24 admixtures must be refrigerated and completely used within 24 ho administration.

HOW SUPPLIED

Novamine® 15% Amino Acids Injection is supplied as a Pharma Package in 500 mL and 1000 mL containers.

500 mL	**NDC** 0338-0494-03
1000 mL	**NDC** 0338-0494-04

STORAGE

Store in the closed carton; do not expose solution to light until r Exposure of pharmaceutical products to heat should be minimizec sive heat. It is recommended that the product be stored at room te (25°C). Brief exposure to temperatures above 25°C during transpo will not adversely affect the product. Solution that has been frozen used.

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