15% Clinisol® - sulfite-free (Amino Acid) Injection

Pharmacy Bulk Package
Not for Direct Infusion

in Viaflex® Plastic Container

Description
15% Clinisol® - sulfite-free (Amino Acid) Injection Pharmacy Bulk Package is a sterile, clear, nonpyrogenic, hypotonic solution of essential and nonessential amino acids. A Pharmacy Bulk Package is a container of a sterile preparation for parenteral use that contains many single doses. The contents are intended for use in a pharmacy admixture program and are restricted to the preparation of admixtures for intravenous infusion.

The Viaflex® plastic container is fabricated from a specially formulated polyvinyl chloride (PL 148® Plastic). Exposure to temperatures 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. The amount of water that can permeate from inside the container to the overwrap is insufficient to affect the solution significantly. Solutions in contact with the plastic container can leach out certain of its chemical components in very small amounts within the expiration period, e.g., 3-2-ethylenedioxypropyl (DEHP), up to 5 parts per million. However, the safety of the plastic has been confirmed in tests in animals according to USP biological test for plastic containers as well as by tissue culture toxicity studies. Each 100 mL of 15% Clinisol® - sulfite-free (Amino Acid) Injection Pharmacy Bulk Package contains:

- **Amino Acids**: 15.0 g
- **Total Nitrogen**: 2.37 g
- **pH (adjusted with glacial acetic acid and may have been adjusted with sodium hydroxide)**: 6.0 (5.0 to 7.0)

Essential Amino Acids
- Lysine - (from Lysine Acetate) C6H14N2O2: 1.18 g
- Leucine - C6H13NO2: 1.04 g
- Phenylalanine - C9H11NO2: 1.04 g
- Valine - C6H13NO2: 960 mg
- Histidine - C6H14N2O2: 894 mg
- Isoleucine - C6H13NO2: 749 mg
- Methionine - C5H11NO2S: 749 mg
- Threonine - C4H9NO2: 749 mg
- Tryptophan - C11H12N2O2: 250 mg

Nonessential Amino Acids
- Alanine - C3H7NO2: 2.17 g
- Arginine - C5H14N2O2: 1.47 g
- Glycine - C2H5NO2: 1.04 g
- Proline - C5H9NO2: 894 mg
- Glutamic Acid - C5H9NO4: 749 mg
- Serine - C3H7NO2: 592 mg
- Aspartic Acid - C3H4NO3: 434 mg
- Tyrosine - C9H11NO2: 39 mg

Anion profiles per liter
- Acetate from Lysine Acetate and glacial acetic acid: 127 mEq
- Sodium chloride: 1357 mEq/L

Clinical Pharmacology

15% Clinisol® - sulfite-free (Amino Acid) Injection Pharmacy Bulk Package administered intravenously will provide biologically useful source material for protein synthesis when used with concentrated calorie sources, electrolytes, vitamins and minerals.

Central Infusion
15% Clinisol® - sulfite-free (Amino Acid) Injection Pharmacy Bulk Package is intended for use in a pharmacy admixture program and as such is restricted to the preparation of admixtures for intravenous use. 15% Clinisol® - sulfite-free (Amino Acid) Injection Pharmacy Bulk Package given by central venous infusion in combination with energy sources, vitamins, trace elements and electrolytes, will meet the requirements for weight maintenance or weight gain. The energy component may be derived solely from dextrose or may be provided by a combination of dextrose and intravenous fat emulsion.

Peripheral Infusion
15% Clinisol® - sulfite-free (Amino Acid) Injection Pharmacy Bulk Package, when diluted to an appropriate osmolality level (718 mOsm/L) can also be administered by a peripheral vein when use of a central venous catheter is contraindicated.

Indications and Usage
15% Clinisol® - sulfite-free (Amino Acid) Injection Pharmacy Bulk Package is indicated as an adjunct in the offsetting of nitrogen loss or in the treatment of negative nitrogen balance in patients where: (1) the alimentary tract 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
- Hypersensitivity to one or more amino acids
- Severe liver disease or hepatic coma
- Anuria
- Metabolic disorders involving impaired nitrogen utilization

Warnings
- Admixtures may be incompatible. Consult with pharmacist, if available. When introducing additives, use aseptic techniques. Mix thoroughly. Do not store.
- Because of the potential for life-threatening events, caution should be taken to ensure that pressurized rates have not formed in any parental nutrient admixture.

This injection is for compounding only, not for direct infusion.

Once container closure has been penetrated, withdrawal of contents should be completed within 4 hours. After initial entry, maintain contents at room temperature (25°C/77°F).

Any admixture storage should be under refrigeration and limited to a brief period of time, preferably less than 24 hours.

Administration of amino acid solutions at excessive rates or to patients with hepatic insufficiency may result in plasma amino acid imbalance, hyperammonemia, prerenal acidemia, stupor and coma. Conservative doses of amino acids should be given to these patients, dictated by the nutritional status of the patient. Should symptoms of hyperammonemia develop, amino acid administration should be discontinued and the patient's clinical status reevaluated.

WARNING: This product contains aluminum that may be toxic. Aluminum may reach toxic levels with prolonged parental 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 parental levels of aluminum at greater than 4 to 5 µg/kg/day accumulate aluminum at levels associated with central nervous system and bone toxicity. Tissue loading may occur at even lower rates of administration.

Precautions

General
In order for parenterally administered amino acids to be retained by the body and utilized for protein synthesis adequate calories must be administered concurrently.

The administration of 15% Clinisol® - sulfite-free (Amino Acid) Injection Pharmacy Bulk Package as part of total parenteral nutrition (TPN) with large volumes of hypersonic fluids requires periodic monitoring of the patient for signs of hyperammonemia, hypertriglyceridemia, hyperglycemia, hyperuricemia, and hyperkalemia.

During parenteral nutrition with concentrated dextrose and amino acid solutions, essential fatty acid deficiency syndrome may develop but may not be clinically apparent. Early demonstration of this condition can only be accomplished by analysis of plasma lipids. The syndrome may be prevented or corrected by appropriate treatment with intravenous fat emulsions.
For complete nutritional support, TPN regimens must also include multiple vitamins and trace elements. Potentially incompatible ions such as calcium and phosphate may be added to alternate infusate containers to avoid precipitation.

Initiation and termination of infusions of TPN fluids must be gradual to permit adjustment of endogenous insulin release. Caution should be exercised against volume overload.

Do not administer undiluted solution.

TPN delivered through a central or large peripheral vein is a special technique requiring a team effort by physician, nurse and pharmacist. The responsibility for administering the solution is divided among these three professionals, and the nurse is responsible to the attending physician for the infusion of all drugs, and the pharmacist for all solutions. 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 catheter be accomplished under controlled aseptic conditions.

It is essential that a carefully prepared protocol, based on current medical practices be followed.

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

Laboratory Tests

Frequent clinical evaluations and laboratory determinations are necessary for proper monitoring during administration.

Laboratory tests should include blood glucose, serum electrolytes, liver and renal function, serum osmolality, blood ammonia, serum protein, pH, hematocrit, and WBC.

When 15% Clinisept® - sulfite-free (Amino Acid) Injection Pharmacy Bulk Package 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. Serum electrolytes should be monitored daily.

Carcinogenesis, mutagenesis, impairment of fertility: Long term animal studies with 15% Clinisept® - sulfite-free (Amino Acid) Injection Pharmacy Bulk Package have not been performed to evaluate the carcinogenic potential, mutagenic potential or effects on fertility.

Pregnancy: Teratogenic Effects

Pregnancy Category C: Animal reproduction studies have not been conducted with 15% Clinisept® - sulfite-free (Amino Acid) Injection Pharmacy Bulk Package. It is also not known whether 15% Clinisept® - sulfite-free (Amino Acid) Injection Pharmacy Bulk Package can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. 15% Clinisept® - sulfite-free (Amino Acid) Injection Pharmacy Bulk Package should be given to a pregnant woman only if clearly needed.

Nursing Mothers: Caution should be exercised when 15% Clinisept® - sulfite-free (Amino Acid) Injection Pharmacy Bulk Package is administered to a nursing woman.

Pediatric Use: Safety and effectiveness of 15% Clinisept® - sulfite-free (Amino Acid) Injection in pediatric patients have not been established by adequate and well-controlled studies. However, the use of amino acid 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. See Dosage and Administration.

Adverse Reactions

Local reactions consisting of a warm sensation, erythema, phlebitis and thrombosis at the infusion site have occurred with peripheral intravenous infusion of amino acids. In such cases the infusion site should be changed promptly to another vein. Generalized flushing, fever and nausea also have been reported during peripheral infusions of amino acid solutions.

The following metabolic complications have been reported with administration of TPN: metabolic acidosis and alkalosis, hypophosphatemia, hypocalcemia, osteoporosis, pellagra, hypoglycemia, hyperkalemia, hyperglycemia, hypernatremia, hyponatremia, hypercalcemia, hyperammonemia, and dehydration. Sepsis has been reported following intravenous therapy, especially when using central venous catheters for prolonged periods.

Complications known to occur from the placement of central venous catheters are pneumothorax, hemathorax, hydrothorax, artery puncture and transaction injury to the brachial plexus, malposition of the catheter, formation of arteriovenous fistula, phlebitis, thrombosis and air and catheter embol.

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Dosage and Administration

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 glycocalcium. Similarly, withdrawal should be accomplished gradually to avoid rebound hypoglycemia.

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

Pediatric Use: Use of 15% Clinisept® - sulfite-free (Amino Acid) Injection in pediatric patients is governed by the same considerations that affect the use of any amino acid solution in pediatrics. The amount administered is based on the basis of grams of amino acid/kg of body weight/day. Two to three grams of body weight for infants with adequate calories are generally sufficient to satisfy protein needs and promote positive nitrogen balance. Solutions administered by peripheral vein should not exceed twice the normal serum osmolality (718 mOsm/L).

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration.

A slight yellow color does not alter the quality and efficacy of this product. Additives may be incompatible. Complete information is not available. Those additives known to be incompatible should not be used. Consult with pharmacist, if available. When compounding admixtures, use aseptic technique. Mix thoroughly. Do not store any unused portion of 15% Clinisept® - sulfite-free (Amino Acid) Injection Pharmacy Bulk Package.

Central Vein Infusion

In untrained adult subjects with no unusual nitrogen losses, a minimum dosage of 0.1 gram nitrogen (6.2 ml, of 15% Clinisept® - sulfite-free (Amino Acid) Injection Pharmacy Bulk Package) plus 4.4 grams (15 calories) of dextrose/lipid emulsion per kilogram of body weight per day is required to achieve nitrogen balance and energy balance. 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, 15% Clinisept® - sulfite-free (Amino Acid) Injection Pharmacy Bulk Package) 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 best indicator of proper dosage.

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

Peripheral Infusion

In patients for whom central vein catheterization is not advisable, admixtures with 15% Clinisept® - sulfite-free (Amino Acid) Injection Pharmacy Bulk Package can be administered by peripheral vein. Dilution of 250 ml, 15% Clinisept® - sulfite-free (Amino Acid) Injection Pharmacy Bulk Package in 750 ml of 10% dextrose will reduce the osmolality to a level (718 mOsm/L) which is more favorable to the maintenance of the integrity of the walls of the veins. If infused simultaneously, fat emulsion will provide a dilution effect upon the osmolality, as well. In pediatric patients, the final solution should not exceed twice normal serum osmolality (718 mOsm/L).

Directions for use of Vialtex® plastic PharmacyBulk Container

Do not use overplastic has been previously opened or damaged.

To Open

Tear overplastic at notch and remove solution container. Some opacity of the plastic may be observed and will diminish gradually. Check for minute leaks by squeezing inner bag firm. If leaks are found, discard.

Preparation for Administering

1. The Pharmacy Bulk Package is to be used only in a suitable aseptic work area.

2. Suspend container.

3. Remove plastic protector from port.

4. Attach a suitable sterile transfer device or dispensing set which allows measured dispensing of the contents. Refer to complete directions accompanying device.

5. Vialtex® containers should not be written on directly since ink migration has not been investigated. Affix accompanying label for date and time of entry.

How Supplied

15% Clinisept® - sulfite-free (Amino Acid) Injection Pharmacy Bulk Package is available in Vialtex® plastic containers as follows:

286187 500 ml. NDC 0338-0502-02

286189 2000 ml. NDC 0338-0502-06

Exposure of pharmaceutical products to heat should be minimized. Avoid excessive heat. Protect from freezing. It is recommended the product be stored at room temperature (25°C/77°F).

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Clinical Nutrition Division

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