PRODUCT MONOGRAPH

CLINIMIX E

4.25% Amino Acids (Blend B) with Electrolytes in 10% Dextrose Injection
4.25% Amino Acids (Blend B) with Electrolytes in 25% Dextrose Injection
5% Amino Acids (Blend B) with Electrolytes in 10% Dextrose Injection
5% Amino Acids (Blend B) with Electrolytes in 16.6% Dextrose Injection
5% Amino Acids (Blend B) with Electrolytes in 20% Dextrose Injection
5% Amino Acids (Blend B) with Electrolytes in 25% Dextrose Injection
5% Amino Acids (Blend C) with Electrolytes in 10% Dextrose Injection
5% Amino Acids (Blend C) with Electrolytes in 16.6% Dextrose Injection
5% Amino Acids (Blend C) with Electrolytes in 25% Dextrose Injection

CLINIMIX

4.25% Amino Acids (Blend B) without Electrolytes in 10% Dextrose Injection
4.25% Amino Acids (Blend B) without Electrolytes in 25% Dextrose Injection
5% Amino Acids (Blend B) without Electrolytes in 5% Dextrose Injection
5% Amino Acids (Blend B) without Electrolytes in 10% Dextrose Injection
5% Amino Acids (Blend B) without Electrolytes in 16.6% Dextrose Injection
5% Amino Acids (Blend B) without Electrolytes in 20% Dextrose Injection
5% Amino Acids (Blend B) without Electrolytes in 25% Dextrose Injection
5% Amino Acids (Blend C) without Electrolytes in 10% Dextrose Injection
5% Amino Acids (Blend C) without Electrolytes in 16.6% Dextrose Injection

Amino Acids with or without Electrolytes in Dextrose Injection
Solution for Infusion

Intravenous Nutritive Supplements

Baxter Corporation
Mississauga, Ontario L5N 0C2

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CLINIMIX E / CLINIMIX

Amino Acids with or without Electrolytes in Dextrose Injection

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Clinically Relevant Nonmedicinal Ingredients
Intravenous	Solution for Infusion **CLINIMIX E** 4.25% Amino Acids (Blend B) with Electrolytes in 10% Dextrose Injection 4.25% Amino Acids (Blend B) with Electrolytes in 25% Dextrose Injection 5% Amino Acids (Blend B) with Electrolytes in 10% Dextrose Injection 5% Amino Acids (Blend B) with Electrolytes in 16.6% Dextrose Injection 5% Amino Acids (Blend B) with Electrolytes in 20% Dextrose Injection 5% Amino Acids (Blend B) with Electrolytes in 25% Dextrose Injection 5% Amino Acids (Blend C) with Electrolytes in 10% Dextrose Injection 5% Amino Acids (Blend C) with Electrolytes in 16.6% Dextrose Injection 5% Amino Acids (Blend C) with Electrolytes in 25% Dextrose Injection **CLINIMIX** 4.25% Amino Acids (Blend B) without Electrolytes in 10% Dextrose Injection 4.25% Amino Acids (Blend B) without Electrolytes in 25% Dextrose Injection 5% Amino Acids (Blend B) without Electrolytes in 5% Dextrose Injection 5% Amino Acids (Blend B) without Electrolytes in 10% Dextrose Injection 5% Amino Acids (Blend B) without Electrolytes in 16.6% Dextrose Injection 5% Amino Acids (Blend B) without Electrolytes in 20% Dextrose Injection	None of the nonmedicinal ingredients are clinically relevant. *For a complete listing see Dosage Forms, Composition and Packaging section.*

	5% Amino Acids (Blend B) without Electrolytes in 25% Dextrose Injection 5% Amino Acids (Blend C) without Electrolytes in 10% Dextrose Injection 5% Amino Acids (Blend C) without Electrolytes in 16.6% Dextrose Injection	

INDICATIONS AND CLINICAL USE

CLINIMIX E (Amino Acids with Electrolytes in Dextrose Injection) products and CLINIMIX (Amino Acids without Electrolytes in Dextrose Injection) products are indicated as a source of amino acids and carbohydrate calories in clinical conditions where enteral nutritional supply is or is expected to be insufficient or impossible in order to offset or prevent nitrogen loss or negative nitrogen balance.

Pediatrics:
There have been no studies performed by Baxter Healthcare Corporation in the pediatric population. See **Special Populations, Pediatrics** section regarding monitoring for hyperammonemia in pediatric patients.

Geriatrics:

In general, dose selection for an elderly patient should be cautious, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or drug therapy.

CONTRAINDICATIONS

The use of all formulations of CLINIMIX E / CLINIMIX (Amino Acids with or without Electrolytes in Dextrose Injection) is contraindicated in the following populations / situations:

- Known hypersensitivity to any of the substances or component of the container. For a complete listing, see Table 7 to Table 10 and text in the Dosage Forms, Composition and Packaging section of the Product Monograph.
- Concomitant administration of ceftriaxone in newborns (≤ 28 days of age), even if separate infusion lines are used due to risk of fatal ceftriaxone-calcium salt precipitation in the neonate's bloodstream.
- Simultaneous administration of ceftriaxone through the same infusion line (e.g., via Y-port/Y-site) in patients older than 28 days of age. If the same infusion line is used for sequential administration, the line must be thoroughly flushed between infusions with a compatible fluid.
- CLINIMIX E must not be administered to patients with pathologically elevated plasma concentrations of sodium, potassium, magnesium, calcium and/or phosphorus.

- Known allergy to corn or corn products since the products contain corn-derived dextrose
- Patients with acute renal failure and without undergoing renal replacement therapy.
- Patients with severe liver failure or hepatic coma
- Congenital abnormality of amino acid metabolism
- Severe hyperglycemia (glucose concentration greater than 180 mg/dL or 10 mmol/L)

Additional contraindications specific to all formulations of CLINIMIX E (Amino Acids with Electrolytes Injection in Dextrose Injection):

- Hyperkalemia (see **General** in **WARNINGS AND PRECAUTIONS**)
- Hypercalcaemia (see **General** in **WARNINGS AND PRECAUTIONS**)
- Hyperphosphatemia (see **General** in **WARNINGS AND PRECAUTIONS**)
- Hypernatremia
- Hypermagnesemia
- Co-administration with calcium-containing intravenous solutions (see **General** in **WARNINGS AND PRECAUTIONS**)

WARNINGS AND PRECAUTIONS

General

Proper administration of a CLINIMIX E or CLINIMIX product requires a knowledge of fluid and electrolyte balance nutritional status, nature of the disease, vital organ function as well as clinical expertise in prescribing parenteral nutritional (PN) regimen and recognition and treatment of the complications which may occur.

Immediately prior to addition of additives or infusion, the solutions in the two chambers of the package of a CLINIMIX E or CLINIMIX product must be first mixed together. The mixed solution is called admixed solution in this document.

Compatibility of additives including electrolytes and lipid emulsions with the Admixed solution of a CLINIMIX E or CLINIMIX product must be evaluated before addition to avoid formation of precipitates in the resulting solution. Consult with pharmacist, if available (see **DOSAGE AND ADMINISTRATION** | Dosing Considerations).

If IV lipid emulsion and other additives are to be added to the Admixed solution of a product, the additives must be added before lipid addition to facilitate visual inspection for incompatibility (see Administration subsection in the **DOSAGE AND ADMINISTRATION** section under the subheading *Additives*).

Precipitates in a PN solution may result in life-threatening clinical outcomes (see Respiratory subsection and **ADVERSE REACTIONS** section).

Exercise caution to ensure that precipitates or particulate matter are not formed or present in any solutions before and after preparation of a solution for IV administration. Discard any solution where precipitates, particulate matter, cloudiness, discoloration and/or other unusual appearance are observed.

Due to presence of phosphate ion in CLINIMIX E product (Table 1 and Table 3), administration of these products may result in precipitation of calcium phosphate in patients with hyperphosphatemia, hypercalcaemia and /or co-administrated with a calcium ion-containing IV solution. Addition of calcium-containing agents to the product may result in precipitation.

If an electrolyte is to be added to a CLINIMIX E or CLINIMIX product, the type and amount of the electrolyte should be dictated by the status of electrolyte balance, disease condition and related vital organ function of the patient to avoid over-loading the electrolyte and resulting in serious adverse reactions.

CLINIMIX E products contain high concentration of potassium ion (30 mmol/L, see Table 1 and Table 3), while CLINIMIX products contain no potassium ion (Table 2 and Table 4). When prescribing these products, such features should be taken into account to prevent hyperkalemia for CLINIMIX E products and hypokalemia for CLINIMIX products.

Aseptic techniques are required when additives are added as nutrients in the products support growth of microorganisms.

Severe water and electrolyte disorders, severe fluid overload states, and severe metabolic disorders should be corrected before starting the infusion.

Do not administer unless the final prepared solution is clear. A slight yellow color does not alter the quality and activity of the product.

During infusion, the infused solution inside the plastic container, the infusion tubing and catheter should periodically be checked for precipitates and other unusual appearance (see **DOSAGE AND ADMINISTRATION**). If any unusual appearance is observed, immediately stop the infusion, remove the infusion set and catheter and initiate medical evaluation.

Due to high osmolarity (from 775 to 1907 mOsm/L, See Table 1 to Table 4), CLINIMIX E / CLINIMIX products may result in phlebitic complications, such as vein irritation, vein damage, and thrombosis when administrated via peripheral vein. Therefore, these products are generally administrated via central vein through an indwelling central intravenous catheter with the tip located in the superior vena cava (see DOSAGE AND ADMINISTRATION | Administration).

During the administration of CLINIMIX E or CLINIMIX products, serum potassium concentration should be closely monitored to prevent hyperkalemia in case of CLINIMIX E or hypokalemia in case of CLINIMIX. Administration of CLINIMIX E product must be discontinued if hyperkalemia occurs. Hypokalemia should be prevented or managed in a timely manner if it occurs.

Administration of amino acid solutions and other nutrients via central or peripheral venous catheter may be associated with complications which can be prevented or minimized by careful attention to all aspects of the procedure. This includes 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.

Infection and sepsis may occur as a result of the use of intravenous catheters to administer parenteral formulations, poor maintenance of catheters or contaminated solutions. Immunosuppression and other factors such as hyperglycemia, malnutrition and/or their underlying disease state may predispose patients to infectious complications.

Careful symptomatic and laboratory monitoring for fever/chills, leukocytosis, technical complications with the access device, and hyperglycemia can help recognize early infections.

The occurrence of septic complications can be decreased with heightened emphasis on aseptic technique in catheter placement, maintenance, as well as aseptic technique in nutritional formula preparation.

Refeeding severely undernourished patients may result in the refeeding syndrome that is characterized by the shift of potassium, phosphorus, and magnesium intracellularly as the patient becomes anabolic. Thiamine deficiency and fluid retention may also develop. Careful monitoring and slowly increasing nutrient intakes while avoiding overfeeding can prevent these complications.

During prolonged 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 lipid emulsions.

Infusion of the preparation of CLINIMIX E or CLINIMIX products must not be through the same tubing with blood or blood components unless there is documentation that it is safe.

Do not use plastic containers in series connections. Such use could result in air embolism due to residual air being drawn from the primary container before administration of the fluid from the secondary container is completed.

Cardiovascular

Use with caution in patients with pulmonary edema or heart failure. Fluid status should be closely monitored.

Endocrine and Metabolism

Metabolic complications may occur if the nutrient intake is not adapted to the patient's requirements, or the metabolic capacity of any given dietary component is not accurately assessed. Adverse metabolic effects may arise from administration of inadequate or excessive nutrients or from inappropriate composition of an admixture for a particular patient's needs.

CLINIMIX E/CLINIMIX products may contain fructose. Exercise caution when these products are used in patients with hereditary fructose intolerance due to aldolase deficiency.

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 hyperammonemia (see **Post-Market Adverse Drug Reactions** subsection in **ADVERSE REACTIONS** section). Frequent clinical evaluation and laboratory determinations are necessary, especially during the first few days of therapy, to prevent or minimize these complications.

Depending on extent and etiology, hyperammonemia may require immediate intervention. Should symptoms of hyperammonemia develop, administration should be discontinued and the patient's clinical status re-evaluated.

Hyperammonemia is of special significance in newborns and infants. It is essential that blood ammonia be measured frequently in newborns and infants. In some patients this may indicate the presence of a congenital disorder of amino acid metabolism or hepatic insufficiency.

The IV administration of these solutions can lead to fluid or solute overload resulting in hyper or hypoosmolal states. The risk of hypoosmolal states is especially present in conditions associated with Antidiuretic Hormone (ADH) secretion and is proportional to the infusion rate.

Parenteral administration of these products, especially those containing high concentration of dextrose, may result in hyperglycemia, glycosuria, and hyperosmolar syndrome. Blood and urine glucose should be monitored on a routine basis in patients receiving this therapy to adequately control blood glucose level and prevent serious complications associated with hyperglycemia.

Sudden cessation in administration of a concentrated dextrose solution, such as a CLINIMIX E or CLINIMIX product, may result in rebound hypoglycemia due to continued endogenous insulin production. Parenteral nutrition mixtures should be withdrawn slowly.

Special care must be taken when giving a CLINIMIX E / CLINIMIX product with high dextrose concentration to patients with impaired glucose tolerance such as diabetics or prediabetics and uremic patients, especially when the latter are receiving peritoneal dialysis. To reduce the risk of hyperglycemia-associated complications, the infusion rate must be adjusted and/or insulin administered if blood glucose levels exceed levels considered acceptable for the individual patient.

Handling of glucose load is also frequently impaired in patients with liver failure.

Hepatic/Biliary/Pancreatic

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

Parenteral nutrition in general as well as amino acid solutions should be used with caution

in patients with preexisting liver disease or liver insufficiency. Liver function parameters should be closely monitored in these patients, and they should be monitored for possible symptoms of hyperammonemia (see **Endocrine and Metabolism**). Should symptoms of hyperammonemia develop, administration should be discontinued and the patient's clinical status should be re-evaluated.

Hepatobiliary disorders including cholestasis, hepatic steatosis, fibrosis and cirrhosis, possibly leading to hepatic failure, as well as cholecystitis and cholelithiasis are known to develop in some patients on parenteral nutrition. The etiology of these disorders is thought to be multifactorial and may differ between patients. Patients developing abnormal laboratory parameters or other signs of hepatobiliary disorders should be assessed early by a clinician knowledgeable in liver diseases in order to identify possible causative and contributory factors, and possible therapeutic and prophylactic interventions.

Immune

Anaphylaxis has been reported with other parenteral nutrition products

Hypersensitivity/infusion reactions have been reported with CLINIMIX E or CLINIMIX products (see **CONTRAINDICATIONS** and **ADVERSE REACTIONS** sections**).**

The infusion must be stopped immediately if any signs or symptoms of a hypersensitivity / infusion reaction develop.

Since dextrose in CLINIMIX E / CLINIMIX products is derived from corn, these products should not be used in patients with known allergy to corn or corn products (see CONTRAINDICATIONS section).

Renal

Use with caution in patients with renal insufficiency. Fluid and electrolyte status should be closely monitored for water and/or electrolyte retention.

Azotemia has been reported with parenteral administration of solutions containing amino acids, and may occur in particular in the presence of renal impairment.

Respiratory

Pulmonary vascular precipitates causing pulmonary vascular emboli and pulmonary distress have been reported in patients receiving parenteral nutrition. In some cases, fatal outcomes have occurred mainly due to pulmonary thromboemboli. Although pulmonary vascular precipitates have been reported even in the absence of phosphate salt in the solution, the risk of such reaction is expected to be much higher for a PN solution containing phosphate and/or calcium ions. Excessive addition of calcium and and/or phosphate ions increases the risk of the formation of calcium phosphate precipitates. Precipitation distal to the in-line filter and suspected in vivo precipitate formation has also been reported.

Pulmonary vascular precipitates have been reported with parenteral nutrition products (see ADVERSE REACTIONS section).

If signs of pulmonary distress occur, the infusion must be stopped and medical evaluation

initiated.

Special Populations

Pregnant Women:

There are no adequate data on use of CLINIMIX E / CLINIMIX (Amino Acids with or without Electrolytes in Dextrose Injection) in pregnant women. Healthcare professionals should carefully consider the potential risks and benefits for each specific patient before prescribing the product.

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

Nursing Women:

There are no adequate data on use of CLINIMIX E / CLINIMIX (Amino Acids with or without Electrolytes in Dextrose Injection) in lactating women. Healthcare professionals should carefully consider the potential risks and benefits for each specific patient before prescribing the product.

Pediatrics:

There have been no studies performed by Baxter Healthcare Corporation in the pediatric population. Hyperammonemia is of special significance in newborns and infants. . In some patients this may indicate the presence of a congenital disorder or amino acid metabolism or hepatic insufficiency (see **Endocrine and Metabolism**). Blood ammonia should be measured frequently in newborns and infants to detect hyperammonemia, Should symptoms of hyperammonemia develop, administration should be discontinued and the patient's clinical status shoud be re-assessed.

Geriatrics:

In general, dose selection for an elderly patient should be cautious, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or drug therapy.

Monitoring and Laboratory Tests

CLINIMIX E product contains sufficient electrolytes to provide for most parenteral nutritional needs.However, replacement of exceptional electrolyte loss due to nasogastric suction, fistula drainage, or unusual tissue exudation may be necessary. Particular attention should be given to monitoring serum potassium and phosphate levels.

Patients receiving CLINIMIX product should be carefully monitored and their electrolyte requirements individualized (see **General**).

Monitoring should be appropriate to the patient's clinical situation and condition, and may include determinations of fluid balance, water and electrolyte balance , serum osmolarity, and acid / base balance , blood glucose , serum proteins, blood ammonia levels, kidney and liver function tests, electrolytes, hemogram, arterial blood gases, and blood cultures.

ADVERSE REACTIONS

Adverse Drug Reaction Overview

Adverse reaction information is based on postmarketing experiences.

Post-Market Adverse Drug Reactions

The following adverse reactions have been reported with CLINIMIX E / CLINIMIX formulations in the post-marketing experience, listed by MedDRA System Organ Class (SOC), then by Preferred Term in order of severity, where feasible.

IMMUNE SYSTEM DISORDERS:

Hypersensitivity/infusion reactions, including the following manifestations: Hypotension, Hypertension, Peripheral cyanosis, Tachycardia, Dyspnea, Vomiting, Nausea, Urticaria, Rash, Pruritus, Erythema, Hyperhidrosis, Pyrexia, Chills

Other adverse reactions reported with parenteral nutrition include:

- Anaphylaxis
- Pulmonary vascular precipitates
- Hyperglycemia; Hyperammonemia, Azotemia
- Hepatic failure, Hepatic cirrhosis, Hepatic fibrosis, Cholestasis, Hepatic steatosis, Blood bilirubin increased, Hepatic enzyme increased
- Cholecystitis, Cholelithiasis
- Infusion site thrombophlebitis, Venous irritation (infusion site phlebitis, pain, erythema, warmth, swelling, induration)
- Anaphylactic/anaphylactoid reactions, including skin, gastrointestinal and severe circulatory (shock) and respiratory manifestations as well as other hypersensitivity/infusion reactions, including arthralgia, myalgia, and headache have been reported with TRAVASOL

DRUG INTERACTIONS

Overview

No interaction studies have been performed by Baxter Healthcare Corporation with CLINIMIX E / CLINIMIX (Amino Acids with or without Electrolytes in Dextrose

Injection).

Drug-Drug Interactions
Caution must be exercised when administering these injections to patients receiving corticosteroids or corticotropin.

Because of its high potassium content (30 mmol/L), CLINIMIX E product should be administered with caution in patients treated with agents or products that can cause hyperkalemia or increase the risk of hyperkalemia, such as potassium sparing diuretics (amiloride, spironolactone, triamterene), ACE inhibitors, angiotensin II receptor antagonists, or the immunosuppressants tacrolimus and cyclosporine.

Co-administration or mixing of calcium-containing IV products with a CLINIMIX E product may result in precipitates of calcium phosphate which may lead to serious adverse reactions. (see **CONTRAINDICATION** | Respiratory, **WARNINGS AND PRECAUTIONS** and **ADVERSE REACTIONS**).

Drug-Food Interactions
No drug-food interaction studies have been evaluated.

Drug-Laboratory Interactions
No drug-laboratory interaction studies have been evaluated.

Drug-Lifestyle Interactions
Interactions with lifestyle have not been evaluated.

DOSAGE AND ADMINISTRATION

Dosing Considerations

- CLINIMIX E or CLINIMIX products contain dextrose and one of two sets of amino acids (Blend B or Blend C) (see Table 7 to Table 10) with the dextrose solution and the amino acid (with or without electrolytes) solution contained in separate chambers in the product package (see Administration subsection below). Electrolytes are present in the amino acid solution in CLINIMIX E products (Table 1 and Table 3), but not in CLINIMIX products (Table 2 and Table 4).
- The solutions in the two chambers must be first mixed together (see Administration subsection below) prior to use (see Table 7 to Table 10 for the contents of the products in the resulting Admixed solution).
- Do not infuse the solution packaged in a chamber without prior mixing.
- Consult the subsection *Additives* below when including electrolytes and lipid emulsion.
- Do not add any additives including electrolytes and lipid emulsion until the solutions in the two chambers are thoroughly mixed to reduce the risk of

instability of the resulting solution and formation of precipitates which may result in serious clinical outcomes (see **CONTRAINDICATION**, Respiratory subsection **WARNINGS AND PRECAUTIONS** and **ADVERSE REACTIONS**). Additives must be added before lipid component to facilitate visual inspection for incompatibility.

- Since CLINIMIX E products contain phosphate ions (Table 1 and Table 3), addition of certain cations, especially calcium ions, into the Admixed solution may result in precipitation of phosphate salts which may result in serious clinical outcomes (see **CONTRAINDICATION**, Respiratory subsection **WARNINGS AND PRECAUTIONS** and **ADVERSE REACTIONS**).
- Discard any solution where precipitates, particulate matter, cloudiness, discoloration and/or other unusual appearance are observed.
- CLINIMIX E or CLINIMIX products should be administrated via a central vein, not a peripheral vein, to to reduce the risk of phlebitic complications which can be caused by high osmolarity of the product (see **WARNINGS AND PRECAUTIONS** and Administration subsection below).
- During infusion, the infused solution, infusion set and catheter should periodically be checked for precipitates. If precipitates (particulate matter) are observed, the infusion must be stopped immediately and medical evaluation initiated.
- Adequate measures should be taken to prevent hyperkalemia when CLINIMIX E products are used due to the high potassium concentration of the products (30 mmol/L, see Table 1 and Table 3)

  If electrolytes are to be added to CLINIMIX products, the type and the amount of electrolytes should be dictated by the status of electrolyte balance, disease condition and related vital organ function of the patient.

- For single use only.

- It is recommended that after opening the bag, the contents should be used immediately, and should not be stored for a subsequent infusion

Table 1. The Contents of the Admixed Solution* of CLINIMIX E Amino Acids (Blend B) with Electrolytes in Dextrose Injection

	Admixed solution* of CLINIMIX E (Blend B)					
	4.25% Amino Acids	**4.25% Amino Acids**	**5% Amino Acids**	**5% Amino Acids**	**5% Amino Acids**	**5% Amino Acids**
	10% Dextrose	**25% Dextrose**	**10% Dextrose**	**16.6% Dextrose**	**20% Dextrose**	**25% Dextrose**
Total amino acids (g/L)	42.5	42.5	50	50	50	50
Nitrogen (g/L)	7.2	7.2	8.4	8.4	8.4	8.4
Dextrose (g/L)	100	250	100	166	200	250
Energy:						
Total energy from amino acids and dextrose approx. (kcal/L)	510	1020	540	766	880	1050
Energy from dextrose (kcal/L)	340	850	340	564	680	850
Electrolytes:						
Sodium (mmol/L)	35	35	35	35	35	35
Potassium (mmol/L)	30	30	30	30	30	30
Magnesium (mmol/L mEq/L)	2.5 5	2.5 5	2.5 5	2.5 5	2.5 5	2.5 5
Phosphate (mmol/L mEq/L)	15 30	15 30	15 30	15 30	15 30	15 30
Chloride (mmol/L)	35	35	35	35	35	35
Acetate (mmol/L)	70.5	70.5	75	75	75	75
Osmolarity approx. (mOsm/L)	1082	1837	1152	1487	1659	1907

* See section Administration | *Preparation of the Product for Administration*

Table 2. The Contents of the Admixed Solution* of CLINIMIX Amino Acids (Blend B) without Electrolytes in Dextrose Injection

	Admixed solution* of CLINIMIX (Blend B)						
	4.25% Amino Acids	**4.25% Amino Acids**	**5% Amino Acids**	**5% Amino Acids**	**5% Amino Acids**	**5% Amino Acids**	**5% Amino Acids**
	10% Dextrose	**25% Dextrose**	**5% Dextrose**	**10% Dextrose**	**16.6% Dextrose**	**20% Dextrose**	**25% Dextrose**
Total amino acids (g/L)	42.5	42.5	50	50	50	50	50
Nitrogen (g/L)	7.2	7.2	8.4	8.4	8.4	8.4	8.4
Dextrose (g/L)	100	250	50	100	166	200	250
Energy:							
Total energy approx. (kcal/L) (per 1L bag of Dextrose & Protein)	510	1020	370	540	766	880	1050
Engery from dextrose approx. (kcal/L)	340	850	170	340	564	680	850
Electrolyte:							
Chloride (mmol/L)	17	17	20	20	20	20	20
Acetate (mmol/L)	36.5	36.5	43.5	44	43.5	43.5	43.5
Osmolarity approx. (mOsm/L)	957	1702	775	1005	1362	1534	1782

* See section Administration | *Preparation of the Product for Administration*

Table 3. The Contents of the Admixed Solution* of CLINIMIX E Amino Acids (Blend C) with Electrolytes in Dextrose Injection

	The Admixed solution* of CLINIMIX E (Blend C)		
	5% Amino Acids	**5% Amino Acids**	**5% Amino Acids**
	10% Dextrose	**16.6% Dextrose**	**25% Dextrose**
Total amino acids (g/L)	50	50	50
Nitrogen (g/L)	8.4	8.4	8.4
Dextrose (g/L)	100	166	250
Energy:			
Total energy approx. (kcal/L)	1080	1532	2100
Dextrose (kcal/L)	340	564	850
Electrolyte:			
Sodium (mmol/L)	35	35	35
Potassium (mmol/L)	30	30	30
Magnesium (mmol/L mEq/L)	2.5 5	2.5 5	2.5 5
Phosphate (mmol/L mEq/L)	15 30	15 30	15 30
Chloride (mmol/L)	35	35	35
Acetate (mmol/L)	75	75	75
Osmolarity approx. (mOsm/L)	1132.5	1467.5	1887.5

* See section Administration | *Preparation of the Product for Administration*

Table 4. The Contents of the Admixed Solution* of CLINIMIX Amino Acids (Blend C) without Electrolytes in Dextrose Injection

	The Admixed solution* of CLINIMIX (Blend C)	
	5% Amino Acids	**5% Amino Acids**
	10% Dextrose	**16.6% Dextrose**
Total amino acids (g/L)	50	50
Nitrogen (g/L)	8.4	8.4
Dextrose (g/L)	100	166
Energy:		
Total energy approx. (kcal/L)	1080	1532
Dextrose (kcal/L)	340	564
Electrolyte:		
Chloride (mmol/L)	20	20
Acetate (mmol/L)	43.5	43.5
Osmolarity approx. (mOsm/L)	**1004**	**1339**

*** See section Administration | *Preparation of the Product for Administration***

Recommended Dose and Dosage Adjustment

The maximum daily doses of each constituent of CLINIMIX E / CLINIMIX products (i.e., amino acids and dextrose) should be based on individual nutritional requirements and patient tolerance.

The total daily dose of these solutions depends on the patient's metabolic requirement 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 nitrogen requirements.

Recommended dietary allowances for protein are from approximately 0.8 g/kg of body weight for adults. It must be recognized, however, that protein as well as caloric requirements in traumatized or malnourished patients may be increased substantially. Daily amino acid doses of approximately 1.0 to 1.5 g/kg of body weight for adults and 2 to 3 g/kg of body weight for infants with adequate calories are generally sufficient to satisfy protein needs and promote positive nitrogen balance.

For the initial treatment of trauma or protein calorie malnutrition, higher doses of protein with corresponding quantities of carbohydrate will be necessary to promote adequate patient response to therapy. The severity of the illness being treated is the primary consideration in determining proper dose level. Higher doses, especially in infants, must be accompanied by more frequent laboratory evaluation.

Care should be exercised to ensure the maintenance of proper levels of serum

potassium. It may be necessary to add additional quantities of this electrolyteto the solution, especially to CLINIMIX products, in order to meet the patient's potassium intake needs. Potassium requirements in a PN formulation for generally healthy people with normal losses are 1-2 mmol/kg/day, but should be customized to meet individual patient needs. CLINIMIX E product inherently contains potassium 30 mmol/L, and this should be taken into account prior to any supplemental potassium additions.

In fluid restricted patients (e.g. renal failure), acceptable total daily administration volumes are dependent upon the fluid balance requirements of the patient. Extreme care should be given to prevent fluctuations of blood osmolarity and serum electrolyte concentrations. Frequent and careful monitoring is mandatory when fluid restricted patients are receiving intravenous nutrition.

Electrolyte supplementation for CLINIMIX products may be indicated according to the clinical needs of the patient.

Although CLINIMIX E products contains electrolytes, supplementations may be indicated according to the clinical needs of the patient. Compatibility of the additives with the product must be determined prior to and after the addition (see Administration subsection below).

As indicated on an individual basis, vitamins and trace elements and other components (including lipids) can be added to the regimen to prevent deficiencies and complications from developing (see Administration subsection below).

Missed Dose
In the event of a missed dose, the infusion should be restarted at the recommended dose and flow rate. Doses should NOT be doubled.

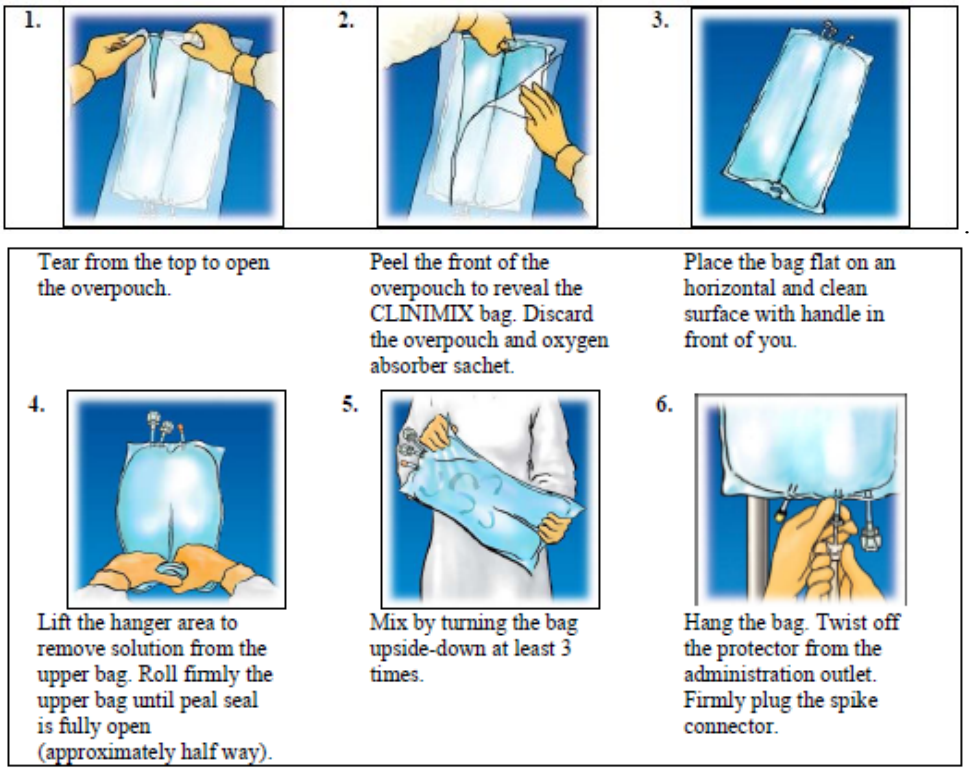
Administration
Preparation of the Product for Administration
Prior to use, the solutions in the two chambers must be thoroughly mixed following the procedure described below. Any additives including electrolytes and lipid emulsion, if needed, should only be added to the mixed solution of the product. For details on the product packaging, see DOSAGE AND ADMINISTRATION | Dosing Considerations and DOSAGE FORMS, COMPOSITION AND PACKAGING section.

Before Mixing:

- Do not open the overwrap until ready for use. The overwrap is not a sterility barrier. The inner bag maintains the sterility of the product.
- Prior to use, tear the overwrap down side at strip and take out the dual-chamber solution container (see Step 1 and Step 2 in Figure 1).
- Confirm that the content of the individual chambers is clear, colorless or slightly yellow. Otherwise, discard the solution and report to Baxter Healthcare Corporation.
- Confirm that the seal between chambers is intact, i.e. solutions are contained in separate

chambers. Check for minute leaks by separately squeezing each chamber. If external leaks or leakage between the chambers are found, discard the solution.

Figure 1. Procedure to prepare the Admixed solution of a CLINIMIX E or CLINIMIX product.



To Mix Solutions:

As shown in Step 3 and Step 4 in Figure 1, lay the dual chamber bag onto a flat surface. Grasp the container firmly on each side of the top of the bag. Starting from the top squeeze and roll bag to open seal between chambers until the inter-chamber seal is completely broken . If the seal has not been separated completely, flip the bag over and repeat process. Ensure that the seal has been opened and the contents of both chambers are thoroughly mixed . Check for leaks.

The mixed solution should be clear and colorless or slightly yellow. Discard the mixed solution and report to Baxter Healthcare Corporation when precipitates, particulate matter, cloudiness, discoloration and/or other unusual appearance are observed.

Lipid emulsion or other additives may be added, but ONLY to the mixed solution following the requirements presented under the subheading “Additives” in this section.

Additives:

The plastic chambers of the product package are made of a non-PVC lipid compatible

material. If required, a lipid emulsion and/or other additives may be injected to the chamber.

Prior to and after the addition, compatibilities and stability of the resulting solution must be checked prior to the addition and further determined after the addition following the procedure "To perform an addition:" described below.

Ensure that the resulting solution is stable after an IV lipid emulsion is added. The prime destabilizers of lipid emulsions are excessive acidity (low pH) and inappropriate electrolyte concentration, particularly divalent cations (Ca^{++} and Mg^{++}). The concentration of all components should not exceed recommended guidelines. Consult a pharmacist if available.

In any parenteral nutritional regimen, calcium and phosphate ratios must be considered. Excess addition of calcium and phosphate, especially in the form of mineral salts, may result in the formation of calcium phosphate precipitates which may result in serious clinical outcomes (see **WARNINGS AND PRECAUTIONS**, Respiratory).

There is no calcium ion in CLINIMIX E/CLINIMIX products. However, CLINIMIX E products contain phosphate ion (Table 1 to Table 4). Caution must be exercised when calcium ion and/or phosphate ion is to be added to the products, especially CLINIMIX E products, to ensure the compatibility to prevent formation of calcium phosphate precipitates. The stability of the resulting solution must be checked.

To perform an addition:

1) Aseptic conditions must be observed.
2) Ensure stability and compatibility of additives.
3) Thoroughly mix the solutions in the dual chambers of the product package together (see Preparation of the Product for Administration subsection).
4) Prepare the injection site of the bag.
5) Puncture the injection site and inject the additives using an injection needle or a reconstitution device (see step #8 for lipid addition).
6) Mix content of the bag and the additives thoroughly.
7) Inspect final solution for discoloration and particulate matter or other incompatibilities.
8) If a lipid emulsion is needed, it should be the last addition made to allow for visual inspection. Repeat Steps 5 through 7 to add the lipid emulsion and check for incompatibilities.
9) Check bag for leaks.
10) Discard the solution whenever discoloration, cloudiness, precipitates, particulate matter and/or leaks are observed.

11) Ensure proper storage requirements of additives are followed.

Method of Administration

Due to high osmolarity of the mixed solution (from 775 to 1907 mOsm/L, See Table 1 to Table 4), the products should be infused via central vein to reduce the risk of phlebitic complications (see General in **WARNINGS AND PRECAUTIONS**).

After appropriate dilution, the products may be infused via peripheral vein if the central venous route is not appropriate (see below for details).

Central Vein Administration: Hypertonic mixtures of amino acids and dextrose may be administered safely by continuous infusion through a central vein catheter with the tip located in the vena cava. In addition to meeting nitrogen needs, the administration rate is governed, especially during the first few days of therapy, by the patient's tolerance to dextrose. Daily intake of amino acids and dextrose should be increased gradually to the maximum required dose as indicated by frequent determinations of urine and blood sugar levels.

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.

Parenteral nutrition may be started with infusates containing lower concentrations of dextrose; dextrose content may be gradually increased to estimated caloric needs as the patient's glucose tolerance increases.

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

Peripheral Vein Administration: The osmolarity of a specific infusion solution must be taken into account when peripheral administration is considered. In adult patients, the final solution should be below 900 mOsm/L. The osmolarity of majority of the CLINIMIX E/CLINIMIX products exceed this level (from 775 to 1907 mOsm/L see Table 1 to Table 4). Therefore, for patients who require parenteral nutrition and in whom the central vein route is not indicated, these solutions should be diluted accordingly and then infused by peripheral vein. Sterile water for injection or sterile dextrose solution for injection with low concentration of dextrose may be used for dilution.

Administration

Depending upon the clinical condition of the patient, approximately 3 litres of parenteral nutrition solution may be administered per 24 hour period. When used postoperatively, the therapy should begin with 1000 mL on the first postoperative day. Thereafter, the dose may be increased to 3000 mL per day.

The rate of administration should be adjusted according to the dosage, the characteristics of

the infused solution, the total volume intake per 24 hours and the duration of the infusion. The infusion time should be 12 to 24 hours.

The flow rate should be increased gradually. The flow rate must be adjusted taking into account the dose being administered, the daily volume intake, and the duration of the infusion. To reduce the risk of hypoglycemia after discontinuation, a gradual decrease in flow rate of administration should be considered.

Use of a final filter is recommended during administration of all parenteral nutrition solutions, where possible. For administration of parenteral solutions without lipids, a 0.22 micron filter should be used. If a lipid is also administered, then a 1.2 micron filter should be used.

During infusion, periodically and carefully inspect the infused solution inside the plastic container, the infusion tubing and catheter for precipitates. If precipitates (particulate matter) are observed, immediately stop the infusion, remove the infusion set and catheter, initiate medical evaluation and report to Baxter Healthcare Corporation.

The prepared product solution is for single use only Do not reconnect any partially used bag.

Careful attention must be given to the proper care of the intravenous catheter to avoid contamination of the blood and consequent septicemia. If fever develops, consider discontinuing therapy and removing catheter. Blood cultures should be taken and the remainder of the fluid saved for examination when deemed necessary.

It is recommended that all intravenous administration apparatus be replaced at least every 24 hours.

CLINIMIX E / CLINIMIX (Amino Acids with or without Electrolytes in Dextrose Injection) must not be infused through the same tubing with blood or blood components unless there is documentation that it is safe.

OVERDOSAGE

For suspected cases of drug overdose, contact the regional Poison Control Centre.

In the event of inappropriate administration (overdose, and/or infusion rate higher than recommended), hyperammonemia, hypervolemia, electrolyte disturbances or acidosis and/or azotemia may occur and result in severe or fatal consequences. In such situations, the infusion must be stopped immediately. If medically appropriate, further intervention may be indicated. See **WARNINGS AND PRECAUTIONS**.

Hyperglycemia, glucosuria, and hyperosmolar syndrome may develop if dextrose infusion

rate exceeds clearance.

There is no specific antidote for overdose. Emergency procedures should include appropriate corrective measures, with particular attention to respiratory and cardiovascular systems.

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

Scientifically, when CLINIMIX E / CLINIMIX (Amino Acids with or without Electrolytes in Dextrose Injection) is administered, nitrogen balance is improved. Maximal nitrogen utilization is promoted by providing adequate calories to meet metabolic needs, usually at least 168 kJ/kg/day (40 kcal/kg/day).

CLINIMIX E / CLINIMIX products provide essential and nonessential amino acids for protein synthesis and dextrose as a source of calories to improve nitrogen balance in malnutrtion or certain disease conditions. In addition, CLINIMIX E products also provide electrolytes including sodium, potassium and phosphate ions to meet individual patient's needs. (See Table 1 and Table 3 for the composition of the products).

Pharmacodynamics

There have been no pharmacodynamic studies performed by Baxter Healthcare Corporation.

Pharmacokinetics

There have been no pharmacokinetic studies performed by Baxter Healthcare Corporation.

Special Populations and Conditions

There have been no clinical pharmacology studies performed by Baxter Healthcare Corporation in special populations and conditions.

STORAGE AND STABILITY

The dosage forms packaged in dual chamber Clarity plastic containers should be stored at temperatures between 15°C and 25°C protected from light and kept from freezing. The prepared amino acids/dextrose admixture should be administered immediately. If not, it should be stored under refrigeration (2° - 8°C) and used within 24 hours.

Mix thoroughly when additives have been introduced. Do not store solutions containing additives.

Mixing calcium-containing IV products with CLINIMIX E products may result in precipitation of calcium phosphate which may lead to serious adverse reactons (see **CONTRAINDICATION**, **WARNINGS AND PRECAUTIONS**, Respiratory and **ADVERSE REACTIONS**).

DOSAGE FORMS, COMPOSITION AND PACKAGING

CLINIMIX E or CLINIMIX products are solutions for injection packaged in a dual chamber container system. The dual chamber product containers are made of a non-PVC, lipid compatible material. Lipid emulsion may be added to the chamber if required.

The left chamber contains Dextrose Injection, while the right chamber contains Amino Acid Injection with electrolytes (in CLINIMIX E) or without electrolytes (in CLINIMIX). The products are available in two different amino acid blends (Blend B and Blend C).

The available package sizes of CLINIMIX E products and CLINIMIX products are listed in Tables 5 and 6, respectively. Composition of the admixed solutions of CLINIMIX E or CLINIMIX products, in either amino acid Blend B or amino acid Blend C, are provided in Tables 7 to 10.

Table 5. Package sizes of CLINIMIX E (Amino Acids with Electrolytes in Dextrose Injection) Products

Product Description	Volume of Admixed solution*	Packaged solution volume in a chamber of a CLINIMIX E product	
		Amino Acids with electrolytes	Dextrose
Amino Acids – Blend B			
4.25% Amino Acids (Blend B) with Electrolytes in 10% Dextrose Injection	1000 mL	500 mL	500 mL
4.25% Amino Acids (Blend B) with Electrolytes in 25% Dextrose Injection	1000 mL	500 mL	500 mL
5% Amino Acids (Blend B) with Electrolytes in 10% Dextrose Injection	1000 mL	500 mL	500 mL
5% Amino Acids (Blend B) with Electrolytes in 16.6% Dextrose Injection	1000 mL	500 mL	500 mL
5% Amino Acids (Blend B) with Electrolytes in 20% Dextrose Injection	1000 mL	500 mL	500 mL
5% Amino Acids (Blend B) with Electrolytes in 25% Dextrose Injection	1000 mL	500 mL	500 mL
Amino Acids – Blend C			
5% Amino Acids (Blend C) with Electrolytes in 10% Dextrose Injection	2000 mL	1000 mL	1000 mL
5% Amino Acids (Blend C) with Electrolytes in 16.6% Dextrose Injection	2000 mL	1000 mL	1000 mL
5% Amino Acids (Blend C) with Electrolytes in 25% Dextrose Injection	2000 mL	1000 mL	1000 mL

*Package size is based on the amount of the admixed solution from the two chambers.

Table 6. Package sizes of CLINIMIX
(Amino Acids without Electrolytes in Dextrose Injection)

Product Description	Volume of Admixed solution*	Packaged solution volume in a chamber of a CLINIMIX product	
		Amino Acids with electrolytes	Dextrose
Amino Acids – Blend B			
4.25% Amino Acids (Blend B) without Electrolytes in 10% Dextrose Injection	1000 mL	500 mL	500 mL
4.25% Amino Acids (Blend B) without Electrolytes in 25% Dextrose Injection	1000 mL	500 mL	500 mL
5% Amino Acids (Blend B) without Electrolytes in 5% Dextrose Injection	1000 mL	500 mL	500 mL
5% Amino Acids (Blend B) without Electrolytes in 10% Dextrose Injection	1000 mL	500 mL	500 mL
5% Amino Acids (Blend B) without Electrolytes in 16.6% Dextrose Injection	1000 mL	500 mL	500 mL
5% Amino Acids (Blend B) without Electrolytes in 20% Dextrose Injection	1000 mL	500 mL	500 mL
5% Amino Acids (Blend B) without Electrolytes in 25% Dextrose Injection	1000 mL	500 mL	500 mL
Amino Acids – Blend C			
5% Amino Acids (Blend C) without Electrolytes in 10% Dextrose Injection	2000 mL	1000 mL	1000 mL
5% Amino Acids (Blend C) without Electrolytes in 16.6% Dextrose Injection	2000 mL	1000 mL	1000 mL

*Package size is based on the amount of the admixed solution from the two chambers.

Table 7. CLINIMIX E (Amino Acids (Blend B) with Electrolytes in Dextrose Injection) Products - Composition of Admixed Solution

	CLINIMIX E (Blend B) Products					
	Composition of the admixed solution					
	4.25% Amino Acids	4.25% Amino Acids	5% Amino Acids	5% Amino Acids	5% Amino Acids	5% Amino Acids
Contents (g/L)*	**10% Dextrose**	**25% Dextrose**	**10% Dextrose**	**16.6% Dextrose**	**20% Dextrose**	**25% Dextrose**
L-Alanine	8.80	8.80	10.40	10.40	10.40	10.40
L-Arginine	4.40	4.40	5.20	5.20	5.20	5.20
Glycine	8.80	8.80	10.40	10.40	10.40	10.40
L-Histidine	1.86	1.86	2.20	2.20	2.20	2.20
L-Isoleucine	2.03	2.03	2.40	2.40	2.40	2.40
L-Leucine	2.63	2.63	3.10	3.10	3.10	3.10
L-Lysine HCl	2.46	2.46	2.90	2.90	2.90	2.90
L-Methionine	2.46	2.46	2.90	2.90	2.90	2.90
L-Phenylalanine	2.63	2.63	3.10	3.10	3.10	3.10
L-Proline	1.78	1.78	2.10	2.10	2.10	2.10
L-Threonine	1.78	1.78	2.10	2.10	2.10	2.10
L-Tryptophan	0.76	0.76	0.90	0.90	0.90	0.90
L-Tyrosine	0.17	0.17	0.20	0.20	0.20	0.20
L-Valine	1.95	1.95	2.30	2.30	2.30	2.30
Dextrose	100	250	100	166	200	250
Electrolytes:						
Sodium Chloride	0.77	0.77	0.585	0.585	0.585	0.585
Sodium Acetate Trihydrate *equivalent to anhydrous salt*	2.97 *1.79*	2.97 *1.79*	3.40 *2.05*	3.40 *2.05*	3.40 *2.05*	3.40 *2.05*
Dibasic Potassium Phosphate	2.61	2.61	2.61	2.61	2.61	2.61
Magnesium Chloride Hexahydrate *equivalent to anhydrous salt*	0.51 *0.24*	0.51 *0.24*	0.51 *0.24*	0.51 *0.24*	0.51 *0.24*	0.51 *0.24*

*Acetic acid glacial is added for pH adjustment

Table 8. CLINIMIX (Amino Acids (Blend B) without Electrolytes in Dextrose Injection) Products - Composition of Admixed Solution

	CLINIMIX (Blend B) Products						
	Composition of the admixed solution						
	4.25% Amino Acids	4.25% Amino Acids	5% Amino Acids	5% Amino Acids	5% Amino Acids	5% Amino Acids	5% Amino Acids
Contents (g/L)*	10% Dextrose	25% Dextrose	5% Dextrose	10% Dextrose	16.6% Dextrose	20% Dextrose	25% Dextrose
L-Alanine	8.80	8.80	10.40	10.40	10.40	10.40	10.40
L-Arginine	4.40	4.40	5.20	5.20	5.20	5.20	5.20
Glycine	8.80	8.80	10.40	10.40	10.40	10.40	10.40
L-Histidine	1.86	1.86	2.20	2.20	2.20	2.20	2.20
L-Isoleucine	2.03	.03	2.40	2.40	2.40	2.40	2.40
L-Leucine	2.63	2.63	3.10	3.10	3.10	3.10	3.10
L-Lysine HCl	2.46	2.46	2.90	2.90	2.90	2.90	2.90
L-Methionine	2.46	2.46	2.90	2.90	2.90	2.90	2.90
L-Phenylalanine	2.63	2.63	3.10	3.10	3.10	3.10	3.10
L-Proline	1.78	1.78	2.10	2.10	2.10	2.10	2.10
L-Threonine	1.78	1.78	2.10	2.10	2.10	2.10	2.10
L-Tryptophan	0.76	0.76	0.90	0.90	0.90	0.90	0.90
L-Tyrosine	0.17	0.17	0.20	0.20	0.20	0.20	0.20
L-Valine	1.95	1.95	2.30	2.30	2.30	2.30	2.30
Dextrose	100	250	50	100	166	200	250

*Acetic acid glacial is added for pH adjustment

Table 9. CLINIMIX E (Amino Acids (Blend C) with Electrolytes in Dextrose Injection) Products - Composition of Admixed Solution

	CLINIMIX E (Blend C) Products		
	Composition of the admixed solution		
	5% Amino Acids	**5% Amino Acids**	**5% Amino Acids**
Contents (g/L)*	**10% Dextrose**	**16.6% Dextrose**	**25% Dextrose**
L-Alanine	10.35	10.35	10.35
L-Arginine	5.75	5.75	5.75
Glycine	5.15	5.15	5.15
L-Histidine	2.4	2.4	2.4
L-Isoleucine	3	3	3
L-Leucine	3.65	3.65	3.65
L-Lysine HCl	2.9	2.9	2.9
L-Methionine	2	2	2
L-Phenylalanine	2.8	2.8	2.8
L-Proline	3.4	3.4	3.4
L-Serine	2.5	2.5	2.5
L-Threonine	2.1	2.1	2.1
L-Tryptophan	0.9	0.9	0.9
L-Tyrosine	0.2	0.2	0.2
L-Valine	2.9	2.9	2.9
Dextrose	100	166	250
Electrolytes:			
Sodium Chloride	0.585	0.585	0.585
Sodium Acetate Trihydrate *equivalent to anhydrous salt*	3.40 *2.05*	3.40 *2.05*	3.40 *2.05*
Dibasic Potassium Phosphate	2.61	2.61	2.61
Magnesium Chloride Hexahydrate *equivalent to anhydrous salt*	0.51 *0.24*	0.51 *0.24*	0.51 *0.24*

*Acetic acid glacial is added for pH adjustment

Table 10. CLINIMIX (Amino Acids (Blend C) without Electrolytes in Dextrose Injection) Products - Composition of Admixed Solution

	CLINIMIX (Blend C) Products	
	Composition of the admixed solution	
	5% Amino Acids	5% Amino Acids
Contents (g/L)*	**10% Dextrose**	**16.6% Dextrose**
L-Alanine	10.35	10.35
L-Arginine	5.75	5.75
Glycine	5.15	5.15
L-Histidine	2.4	2.4
L-Isoleucine	3	3
L-Leucine	3.65	3.65
L-Lysine HCl	2.9	2.9
L-Methionine	2	2
L-Phenylalanine	2.8	2.8
L-Proline	3.4	3.4
L-Serine	2.5	2.5
L-Threonine	2.1	2.1
L-Tryptophan	0.9	0.9
L-Tyrosine	0.2	0.2
L-Valine	2.9	2.9
Dextrose	100	166

*Acetic acid glacial is added for pH adjustment

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION
Drug Substance

CLINIMIX E / CLINIMIX (Amino Acids with or without Electrolytes in Dextrose Injection) contains the following drug substances in two chambers.

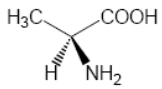
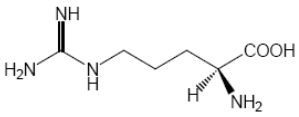
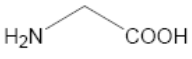
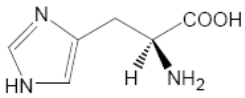
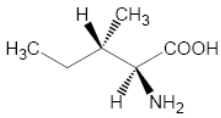
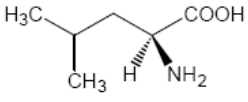
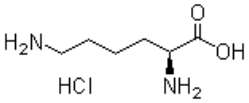
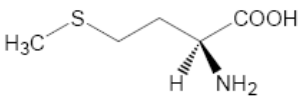
- Dextrose solution (left chamber)
- Amino acid solution with or without electrolytes (sodium, potassium, magnesium, phosphate) (right chamber)

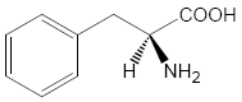
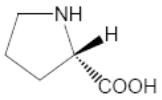
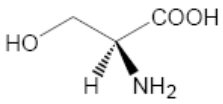
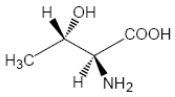
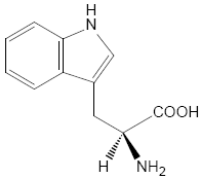
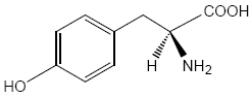
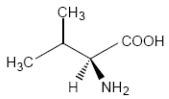
Blends B and C contain the following amino acids:

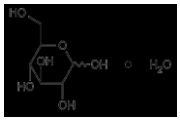
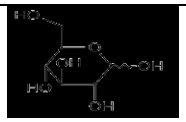
Essential Amino Acids:
L-Histidine, L-Isoleucine, L-Leucine, L-Lysine HCl, L-Methionine, L-Phenylalanine, L-Threonine, L-Tryptophan, L-Valine

Non-Essential Amino Acids:
L-Alanine, L-Arginine, Glycine (Aminoacetic Acid), L-Proline, L-Tyrosine, L-Serine*

* L-Serine is only present in Blend C.

Proper Name Chemical Name	Molecular Formula and Molecular Mass	Structural Formula	Physicochemical Properties
L-Alanine (S)-2-aminopropionic acid	$C_3H_7NO_2$ 89.09		White or almost white crystalline powder or colourless crystals, freely soluble in water, very slightly soluble in alcohol.
L-Arginine (2S)-2-amino-5-guanidinopentanoic acid	$C_6H_{14}N_4O_2$ 174.20		White or almost white crystalline powder or colourless crystals, freely soluble in water, very slightly soluble in alcohol.
Glycine Aminoacetic acid	$C_2H_5NO_2$ 75.07		White or almost white crystalline powder, freely soluble in water, very slightly soluble in alcohol.
L-Histidine (S)-2-amino-1H-imidazole-4-propionic acid	$C_6H_9N_3O_2$ 155.15		White or almost white crystalline powder or colourless crystals, soluble in water, very slightly soluble in ethanol (96%).
L-Isoleucine (2S, 3S)-2-amino-3-methylpentanoic acid	$C_6H_{13}NO_2$ 131.17		White or almost white crystalline powder or flakes, sparingly soluble in water, slightly soluble in alcohol. It dissolves in dilute mineral acids and in dilute solutions of alkali hydroxides.
L-Leucine (2S)-2-amino-4-methylpentanoic acid	$C_6H_{13}NO_2$ 131.17		White or almost white crystalline powder or shiny flakes, sparingly soluble in water, practically insoluble in alcohol. It dissolves in dilute mineral acids and in dilute solutions of alkali hydroxides.
L-Lysine Hydrochloride 2,6 diaminohexanoic acid hydrochloride	$C_6H_{14}N_2O_2 \cdot HCl$ 182.65		White or almost white crystalline powder or colourless crystals, freely soluble in water, very slightly soluble in ethanol.
L-Methionine (2S)-2-amino-4-(methylsulfanyl) butanoic acid	$C_5H_{11}NO_2S$ 149.21		White or almost white crystalline powder or colourless crystals, soluble in water, very slightly soluble in ethanol.

Proper Name Chemical Name	Molecular Formula and Molecular Mass	Structural Formula	Physicochemical Properties
L-Phenylalanine (2S)-2-amino-3-phenylpropanoic acid	$C_9H_{11}NO_2$ 165.19		White or almost white crystalline powder or shiny, white flakes, sparingly soluble in water, very slightly soluble in alcohol. It dissolves in dilute mineral acids and in dilute solutions of alkali hydroxides.
L-Proline (S)-2-pyrrolidinecarboxylic acid	$C_5H_9NO_2$ 115.13		White or almost white crystalline powder or colourless crystals, very soluble in water, freely soluble in alcohol.
L-Serine (S)-2-amino-3-hydroxypropionic acid	$C_3H_7NO_3$ 105.09		White or almost white crystalline powder or colourless crystals, freely soluble in water, practically insoluble in alcohol.
L-Threonine (2S, 3R)-2-amino-3-hydroxybutanoic acid	$C_4H_9NO_3$ 119.12		White crystalline powder or colourless crystals, soluble in water, practically insoluble in ethanol.
L-Tryptophan (2S)-2-amino-3-(indol-3-yl)propanoic acid	$C_{11}H_{12}N_2O_2$ 204.23		White or almost white crystalline or amorphous powder, sparingly soluble in water, slightly soluble in alcohol. It dissolves in dilute mineral acids and in dilute solutions of alkali hydroxides.
L-Tyrosine (S)-2-amino-3-(4-hydroxyphenyl) propionic acid	$C_9H_{11}NO_3$ 181.19		White crystalline powder or colourless crystals, very slightly soluble in water, practically insoluble in alcohol. It dissolves in dilute mineral acids and in dilute solutions of alkali hydroxides.
L-Valine (2S)-2-amino-3-methylbutanoic acid	$C_5H_{11}NO_2$ 117.15		White or almost white crystalline powder or colourless crystals, soluble in water, very slightly soluble in ethanol.
Sodium chloride**	NaCl 58.44	not provided	White crystalline powder, hygroscopic, freely soluble in water, soluble in alcohol.
Sodium acetate trihydrate**	$C_2H_3NaO_2 \cdot 3H_2O$ 136.08		Colourless crystals, very soluble in water, soluble in alcohol.

Proper Name Chemical Name	Molecular Formula and Molecular Mass	Structural Formula	Physicochemical Properties
Potassium Phosphate Dibasic Anhydrous**	K_2HPO_4 174.18	not provided	White or almost white crystalline powder or colourless crystals, freely soluble in water, practically insoluble in anhydrous alcohol.
Magnesium chloride hexahydrate**	$MgCl_2 \cdot 6H_2O$ 203.30	not provided	Colourless crystals, hygroscopic, very soluble in water, freely soluble in alcohol.
Dextrose Monohydrate *** D-glucose monohydrate	$C_6H_{12}O_6 \cdot H_2O$ 198.17		White crystalline powder with a sweet taste, freely soluble in water.
Dextrose Anhyrous*** D-glucose	$C_6H_{12}O_6$ 180.16		White crystalline powder with a sweet taste, freely soluble in water.

* L-Serine is only present in Blend C
** Only contained in the formulations with electrolytes
*** Formulations may contain one of the two types of dextrose

CLINICAL TRIALS

Efficacy and safety have been established by the clinical use of amino acid solutions and dextrose.

DETAILED PHARMACOLOGY

There have been no pharmacology studies performed by Baxter Healthcare Corporation.

TOXICOLOGY

There have been no pharmacology studies performed by Baxter Healthcare Corporation.

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PART III: CONSUMER INFORMATION

CLINIMIX E
(amino acids with electrolytes in dextrose injection) products

CLINIMIX
(amino acids without electrolytes in dextrose injection) products

This leaflet is part III of a three-part "Product Monograph" published when CLINIMIX E (amino acids with electrolytes in dextrose injection) product line and CLINIMIX (amino acids without electrolytes in dextrose injection) product line were approved for sale in Canada. This leaflet is a summary and will not tell you everything about the products. Contact your healthcare professional if you have any questions.

ABOUT THIS MEDICATION

What the medication is used for:
CLINIMIX E (amino acids with electrolytes in dextrose injection) and CLINIMIX (amino acids without electrolytes in dextrose injection) are intravenous nutritive supplements used to provide nutrition through a tube into a vein when normal feeding by mouth is not possible or suitable.

CLINIMIX E / CLINIMIX products must only be used under medical supervision.

What it does:
The use of CLINIMIX E / CLINIMIX products is a way to ensure that patients who are unable to eat get an adequate intake of energy, nitrogen and other nutrients, and helps to treat or prevent malnutrition.

When it should not be used:
CLINIMIX E and CLINIMIX products should not be used if:

- You are allergic to any ingredients (See **What the medicinal ingredients are** and **What the nonmedicinal ingredients are**).
- Your body has problems processing certain amino acids and these amino acids are included in CLINIMIX E / CLINIMIX products.
- You are being administered ceftriaxone.
- You have high plasma concentrations of one of the electrolytes included in CLINIMIX E.
- You have liver failure or coma resulting from liver failure.
- You have kidney failure and are not on dialysis.
- You have hyperglycemia (too much sugar in your blood), which is not controlled.
- You have an allergy to corn or corn products since this product contains dextrose from corn.

Also, CLINIMIX E products should not be used if:

- You have a disorder resulting in high blood levels of substances such as potassium (hyperkalemia), calcium (hypercalcemia), phosphorus (hyperphosphatemia), sodium (hypernatremia) and magnesium (hypermagnesemia).
- You are receiving calcium-containing intravenous solutions.

What the medicinal ingredients are:
CLINIMIX E products and CLINIMIX products are solutions for infusion, each supplied in a bag with two chambers**:**

- one chamber contains a dextrose solution
- one chamber contains a solution of an amino acids:
  Amino acid chamber in CLINIMIX (Blend B) contains: L-alanine, L-arginine, Glycine, L-histidine, L-isoleucine, L-leucine, L-lysine hydrochloride, L-methionine, L-phenylalanine, L-proline, L-threonine, L-tryptophan, L-tyrosine, L-valine

  Amino acid chamber in CLINIMIX E (Blend B) contains: all amino acids listed under CLINIMIX (Blend B) plus electrolytes in the form of sodium chloride, sodium acetate trihydrate, bibasic potassium phosphate and magnesium chloride hexahydrate

  Amino acid chamber in CLINIMIX (Blend C) contains: all amino acids listed under CLINIMIX (Blend B) plus L-Serine

  Amino acid chamber in CLINIMIX E (Blend C) contains: all amino acids listed under CLINIMIX (Blend C) plus electrolytes in the form of sodium chloride, sodium acetate trihydrate, bibasic potassium phosphate and magnesium chloride hexahydrate

What the nonmedicinal ingredients are:
Glacial acetic acid (for pH adjustment), Nitrogen and Water for injection.

What dosage forms it comes in:
CLINIMIX E / CLINIMIX products are solutions for infusion (into the veins). It is supplied in a bag with two chambers. The chambers are separated by a non-permanent seal. Just before administration, the contents of the two chambers are mixed

together by rolling the top of the bag to open the seals.

The mixed solution for each of the different strengths provides a different amount of amino acids, dextrose, and, with some formulations, electrolytes so that your healthcare professional can tailor the infusion to your particular needs.

WARNINGS AND PRECAUTIONS

BEFORE you use CLINIMIX E (amino acids with electrolytes in dextrose injection) or CLINIMIX (amino acids without electrolytes in dextrose injection), talk to your healthcare professional if:

- You are allergic to any ingredients. (See **What the medicinal ingredients are** and **What the nonmedicinal ingredients are**).
- You suffer from metabolic acidosis (when the blood is excessively acid)
- You have kidney or liver problems
- You are taking any other medicines on a regular basis.
- You are pregnant or intend to become pregnant
- You are breastfeeding or intend to breastfeed
- You have pulmonary edema (collection of fluid into the lung tissue)
- You have heart failure
- You have fluid overload (too much water in your body)
- You are diabetic
- You have hereditary fructose intolerance as this product may contain small amounts of fructose.

In all cases, your healthcare professional will base his/her decision to treat you or your child on factors such as age, weight and clinical condition, together with the results of any tests. Always be sure to check with your healthcare professional if anything about your condition changes.

In newborns and infants, your healthcare professional will measure blood ammonia frequently to check for the presence of a congenital abnormality of amino acid metabolism.

If you develop breathing problems during CLINIMIX E / CLINIMIX treatment, contact you doctor immediately.

Your healthcare professional will need to monitor how you are doing while you are on this intravenous nutritive supplement. This means that you will need to have laboratory tests done on a routine basis.

INTERACTIONS WITH THIS MEDICATION

No drug interaction studies have been done with CLINIMIX E (amino acids with electrolytes in dextrose injection) or CLINIMIX (amino acids without electrolytes in dextrose injection).

CLINIMIX E / CLINIMIX products must NOT be administered simultaneously with blood through the same infusion tubing.

Let your healthcare professional know if you are receiving corticosteroids or corticotropin.

There may be interactions between the nutrients in CLINIMIX E / CLINIMIX products and one or more of your medications, for example diuretics, blood pressure drugs, or drugs used to suppress your immune system. You should review your medications with your healthcare professional.

PROPER USE OF THIS MEDICATION

Usual dose:
Your healthcare professional will select the best CLINIMIX E (amino acids with electrolytes in dextrose injection) or CLINIMIX (amino acids without electrolytes in dextrose injection) product for you, based on your age and body weight. Your healthcare professional will ensure that you are getting sufficient calories so that the amino acids from TRAVASOL E (amino acids with electrolytes injection) and TRAVASOL (amino acids without electrolytes injection) will be absorbed. Your healthcare professional will also specify a flow rate corresponding to your needs and medical condition.

Overdose:
If your dose is too high or is infused too quickly, the amino acid content may make your blood too acid, or the dextrose content may increase the glucose in your blood and urine. Giving too high a volume may cause fluid overload.

To prevent these events occurring, your healthcare professional will regularly monitor your condition and test your blood and urine parameters.

In case you feel you have been administered too much CLINIMIX E / CLINIMIX products, contact your healthcare practitioner (e.g. healthcare professional), hospital emergency

department or the regional poison control centre, even if there are no symptoms.

Missed Dose:

If you feel a dose has been missed contact your attending healthcare professional.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

If you notice any changes in the way you feel during or after the treatment, tell your healthcare professional or another member of your medical team immediately.

The tests your healthcare professional will perform while you are taking the intravenous nutritive supplement should reduce the risk of side effects.

If any symptoms of an allergic reaction develop, such as fever or chills, shivering, skin rashes, severe headache or breathing difficulties, contact your attending healthcare professional immediately.

Other side effects may include rapid heart beat, sweating, nausea, and vomiting.

If any side effect gets serious, or if you notice any side effect not listed in this leaflet, please tell your healthcare professional or a member of your medical team right away.

Occasional reddening and stinging may occur at the point where the tubing enters the body. If this occurs, tell your healthcare professional or nurse immediately.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk with your healthcare professional		Stop the infusion and contact your doctor (or healthcare professional)
		Only if severe	In all cases	
Uncommon	Allergic reactions with symptoms such as fever or chills, shivering, skin rashes, breathing difficulties, severe headache			√

This is not a complete list of side effects. For any unexpected effects while taking CLINIMIX E (amino acids with electrolytes in dextrose injection) and CLINIMIX (amino acids without electrolytes in dextrose injection), contact your healthcare professional.

HOW TO STORE IT

The heatlhcare professional will store the CLINIMIX E / CLNIMIX product at temperatures between 15°C and 25°C**,** protected from light and kept from freezing.
Once the seals between the chambers have been broken and the product has been mixed, it should be administered to you **immediately**.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at www.healthcanada.gc.ca/medeffect
- Call toll-free at 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and:
  - Fax toll-free to 1-866-678-6789, or
  - Mail to: Canada Vigilance Program
    Health Canada
    Postal Locator 0701E
    Ottawa, Ontario K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be obtained by contacting the sponsor, Baxter Corporation, at 1-888-719-9955.

This leaflet was prepared by Baxter Corporation, Mississauga, Ontario L5N 0C2, Canada.

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