INDICATIONS

CLINIMIX (amino acids in dextrose) Injections and CLINIMIX E (amino acids with electrolytes in dextrose with calcium) Injections are indicated as a source of calories and protein (and electrolytes for CLINIMIX E) for patients requiring parenteral nutrition when oral or enteral nutrition is not possible, insufficient, or contraindicated. CLINIMIX and CLINIMIX E may be used to treat negative nitrogen balance in patients.

Please see inside back cover for Indications and Important Risk information.

Please see accompanying Package Inserts for full Prescribing Information.
A Premix Option for Flexible PN Therapy

**CLINIMIX and CLINIMIX E Injections.** Source of calories and protein (and a source of electrolytes for CLINIMIX E) in a lipid compatible container.

- The CLINIMIX E Injections formulations are consistent with A.S.P.E.N. electrolyte dosing guidelines for adult patients.¹ ²

Please see inside back cover for Indications and Important Risk information. Please see accompanying Package Inserts for full Prescribing Information.
CLINIMIX and CLINIMIX E Injections can provide adequate nutrients, lipid flexibility, and are available in multiple formulations

**Essential Protein**
- Up to 100 grams of protein/2L bag — highest concentration of protein/L in premix bag

**Lipid Flexibility**
- Underfilled bag allows for the addition of lipids to the bag or, can deliver lipids separately via IV piggyback

**Multiple Formulations**
- Central and peripheral formulations; 1 and 2-liter volumes
- With and without electrolytes
- 78% of custom compounded adult formulations can be met by the use of CLINIMIX Injection products
- Can be used in pediatric and adult patients
- Extended shelf life:
  - 2 years room temperature (while in overwrap)
  - 9 days under refrigeration out of overwrap (or activated with no additives)

**Quality Manufacturing Process**
- Manufactured under cGMP processes, to ensure the identity, strength, quality, and purity of the drug products
- Terminally sterilized; terminally sterilized products represent the lowest risk of microbial contamination for sterile pharmaceutical products (USP<1022>)
- Not made with natural rubber latex

Please see inside back cover for Indications and Important Risk information. Please see accompanying Package Inserts for full Prescribing Information.
Flexible Lipid Addition

The nutritional needs of your patients will be different based on how critically ill they may be. **CLINIMIX** sulfite-free (Amino Acid in Dextrose) Injections and **CLINIMIX E** (amino acids with electrolytes in dextrose with calcium) Injections gives you the power to choose when and how to provide IV fat emulsions.

For 2-in-1 therapy, **CLINIMIX** (amino acids in dextrose) Injections and **CLINIMIX E** (amino acids with electrolytes in dextrose with calcium) Injections may be admixed in the pharmacy and lipids may be piggybacked at the appropriate time during infusion. Infusing lipids separately also allows a visual check for precipitates and particulate matter prior to administration.

For 3-in-1 therapy, lipids can be directly added to the **CLINIMIX** and/or **CLINIMIX E** Injections bag.

Managing Electrolytes

Standardized Parenteral Nutrition (PN) with Electrolytes can be an appropriate choice.

- A.S.P.E.N. suggests managing short-term fluid and electrolyte abnormalities with parenteral nutrition is inappropriate.\(^2\)
- Managing additional electrolyte needs outside of the parenteral nutrition bag is recommended
- A.S.P.E.N. PN Safety Summit recommends standardization of parenteral nutrition formulation processes.\(^6\)

Metabolic complications have been reported, such as acid-base, electrolyte, and blood glucose imbalances, elevated liver enzymes, osmotic diuresis and dehydration.

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>A.S.P.E.N. Daily Electrolyte Guidelines for Adult Parenteral Nutrition(^{**})</th>
<th>CLINIMIX E Injections 2 Liter Bag Contains(^{**})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium</td>
<td>10–15 mEq</td>
<td>9 mEq</td>
</tr>
<tr>
<td>Magnesium</td>
<td>8–20 mEq</td>
<td>10 mEq</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>20–40 mmol</td>
<td>30 mmol</td>
</tr>
<tr>
<td>Sodium</td>
<td>1–2 mEq/kg</td>
<td>70 mEq</td>
</tr>
<tr>
<td>Potassium</td>
<td>1–2 mEq/kg</td>
<td>60 mEq</td>
</tr>
</tbody>
</table>

* Individual dosing needs vary.
** Product codes: 2B7713, 2B7714, 2B7716, 2B7717, 2B7719, 2B7721, 2B7722 and 2B7723

An Essential Component of Your Dual PN System

Custom compounding may be essential for certain high risk patient populations. However, supplementing your compounding operations with premix nutrition delivers additional flexibility:

- Eliminates the delay to starting PN therapy for orders arriving on weekends or orders received after cutoff times
- Immediately available in disaster situations
- Extended shelf life minimizes risk of expiration prior to use
- In a 2006 A.S.P.E.N. survey of PN ordering and compounding, 60% of those surveyed reported 1–5 errors per month related to PN.\(^7\)
- Standardizing PN formulas may help improve clinician prescribing of a balanced formula to help meet patient nutritional goals.\(^8\)

Please see inside back cover for Indications and Important Risk information. Please see accompanying Package Inserts for full Prescribing Information.
Eliminate Manual Calculations with ABACUS Order Entry and Calculation Software

ABACUS Software simplifies the ordering, calculation and labeling process. It conducts up to 17 safety checks, helping to minimize the risk of errors during the formulation ordering process.

ABACUS Software supports the ordering of premixed solutions for parenteral nutrition. Users simply select a premix template, enter the volume and choose a formula. ABACUS Software automatically calculates the infusion rate and duration.

- Additives are calculated and documented within the software
- Printed Label includes all ingredients; premix components + additives
- Eliminates the need for manual calculations
- Ability to calculate overfill and unused volume for Premix orders
- Ability to create multiple order templates for Home Infusion/Alternate Care facilities

The ABACUS Software is intended as an adjunct tool for pharmacy practice. It is not intended to replace the professional judgement or knowledge of a pharmacist or pharmacy technician.

Please see inside back cover for Indications and Important Risk information. Please see accompanying Package Inserts for full Prescribing Information.
Ask for Your PN Order Analysis Today

A PN order analysis can help determine not only if these products will meet your needs, but also which product codes might be most appropriate for your patients’ requirements.

Data shows that **78% of adult PN orders could be filled by CLINIMIX Injections formulas**\(^1\) based on daily needs of:

- Protein
- Calories
- Volume

*Maintenance vitamins, additional electrolytes, and trace elements are not included and should be administered as required.*

\(^1\) 56,672 TPN orders analyzed over 1,000 facilities. Formulas considered a match if within 10% of target. Does not include CLINIMIX E formulations.

---

**Over 15 Years of Customer Satisfaction**

More than 4789 U.S. Healthcare facilities have used CLINIMIX and/or CLINIMIX E Injections

Over 6.5 million bags manufactured and sold in the U.S.


---

Please see inside back cover for Indications and Important Risk information. Please see accompanying Package Inserts for full Prescribing Information.
**INDICATIONS**

CLINIMIX (amino acids in dextrose) Injections and CLINIMIX E (amino acids with electrolytes in dextrose with calcium) Injections are indicated as a source of calories and protein (and electrolytes for CLINIMIX E) for patients requiring parenteral nutrition when oral or enteral nutrition is not possible, insufficient, or contraindicated. CLINIMIX and CLINIMIX E may be used to treat negative nitrogen balance in patients.

**IMPORTANT RISK INFORMATION**

- CLINIMIX and CLINIMIX E Injections are contraindicated in patients with known hypersensitivity to one or more amino acids or dextrose; in patients with inborn errors of amino acid metabolism due to risk of severe metabolic and neurologic complications; and in patients with pulmonary edema or acidosis due to low cardiac output. In addition, CLINIMIX E is contraindicated in neonates (less than 28 days of age) receiving concomitant treatment with ceftriaxone, even if separate infusion lines are used, due to the risk of fatal ceftriaxone calcium salt precipitation in the neonate’s bloodstream.

- Pulmonary vascular precipitates causing pulmonary vascular emboli and pulmonary distress have been reported in patients receiving parenteral nutrition. Excessive addition of calcium and phosphate increases the risk of the formation of calcium phosphate precipitates. The solution should be inspected for precipitates before admixing, after admixing, and again before administration. If signs of pulmonary distress occur, stop the infusion and initiate a medical evaluation.

- Precipitation of ceftriaxone-calcium can occur when ceftriaxone is mixed with CLINIMIX E, in the same intravenous administration line. Do not administer ceftriaxone simultaneously with CLINIMIX E via a Y-site.

- Stop infusion immediately and treat patient accordingly if signs or symptoms of a hypersensitivity reaction develop.

- Monitor for signs and symptoms of early infections.

- Refeeding severely undernourished patients may result in refeeding syndrome. Thiamine deficiency and fluid retention may also develop. Monitor severely undernourished patients and slowly increase nutrient intakes.

- CLINIMIX and CLINIMIX E solutions containing more than 5% dextrose have an osmolarity of ≥ 900 mOsm/L and must be infused through a central catheter.

- CLINIMIX and CLINIMIX E contain no more than 25 mcg/L of aluminum which may reach toxic levels with prolonged administration in patients with renal impairment. Preterm infants are at greater risk because their kidneys are immature, and they require large amounts of calcium and phosphate solutions which contain aluminum. Patients with renal impairment, including preterm infants, who receive parenteral levels of aluminum at greater than 4 to 5 mcg/kg/day, accumulate aluminum at levels associated with central nervous system and bone toxicity. Tissue loading may occur at even lower rates of administration.

- Parenteral Nutrition Associated Liver Disease (PNALD) has been reported in patients who receive parenteral nutrition for extended periods of time, especially preterm infants. If CLINIMIX and CLINIMIX E treated patients develop liver test abnormalities consider discontinuation or dosage reduction.

- Use CLINIMIX and CLINIMIX E with caution in patients with cardiac insufficiency or renal impairment due to increased risk of electrolyte and fluid volume imbalance.

- Monitor renal and liver function parameters, ammonia levels, fluid and electrolyte status, serum osmolarity, blood glucose, blood count and coagulation parameters throughout treatment. In situations of severely elevated electrolyte levels, stop CLINIMIX and CLINIMIX E until levels have been corrected.

- Adverse reactions include diuresis, extravasation, glycosuria, hyperglycemia, and hyperosmolar coma.

Please see accompanying Package Inserts for full Prescribing Information.
Conversion is Easy

Thousands of hospitals have successfully incorporated CLINIMIX (amino acids in dextrose) Injections and CLINIMIX E (amino acids with electrolytes in dextrose with calcium) Injections into their pharmacy operations. Baxter can assist you with all aspects of your conversion process.

- Product Education; inservicing; tools and resources to inform and support the implementation process
- Help identify formulations by conducting a TPN Order Analysis of a sampling of your historical PN orders to determine the most appropriate CLINIMIX and CLINIMIX E formulations
- Bag activation training video and poster; available at www.baxtermedicationdeliveryproducts.com

Place your order now. Call your Baxter representative at 1-888-229-0001
Visit www.clinimix.com

Your global PN leader for more than 80 years.

Please see inside back cover for Indications and Important Risk information.
Please see accompanying Package Inserts for full Prescribing Information.

www.baxter.com

Baxter Healthcare Corporation
One Baxter Parkway
Deerfield, IL 60015

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HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use CLINIMIX safely and effectively. See full prescribing information for CLINIMIX.

CLINIMIX (amino acids in dextrose) injection, for intravenous use Initial U.S. Approval: 1997

INDICATIONS AND USAGE
CLINIMIX is indicated as a source of calories and protein for patients requiring parenteral nutrition when oral or enteral nutrition is not possible, insufficient, or contraindicated. CLINIMIX may be used to treat negative nitrogen balance in patients. (1)

CONTRAINDICATIONS
- Known hypersensitivity to one or more amino acids or dextrose. (4)
- Inborn errors of amino acid metabolism. (4)
- Patients with pulmonary edema or acidosis due to low cardiac output. (4)

WARNINGS AND PRECAUTIONS
- Pulmonary Embolism due to Pulmonary Vascular Precipitates: if signs of pulmonary distress occur, stop the infusion and initiate a medical evaluation. (5.1)

DOSEAGE AND ADMINISTRATION
1. Open by tearing protective foil overwrap across top at slit and remove solution container.
2. For single dose only. Discard unused portion.
3. Attach solution container to administration set. Refer to complete directions accompanying set.
4. c. Attach administration set. Refer to complete directions accompanying set.
5. Once the bag is mixed, check for leaks.
6. Once the bag is mixed, check for leaks.
7. Make additions (if prescribed).
8. Inspect final solution for discoloration and particulate matter. Check for leaks.
9. S. Spike and hang bag.

CONTRAINDICATIONS
- Known hypersensitivity to one or more amino acids or dextrose. (4)
- Inborn errors of amino acid metabolism. (4)
- Patients with pulmonary edema or acidosis due to low cardiac output. (4)

DOSEAGE FORMS AND STRENGTHS
- For central vein infusion only: CLINIMIX 4.25/10, 4.25/20, 4.25/25, 5/15, 5/20, 5/25
- For central or peripheral vein infusion: CLINIMIX 2.75/5 and 4.25/5

DOSEAGE AND ADMINISTRATION
2. Preparation Prior to Administration
- Tear protective foil overwrap across top at slit and remove solution container. Small amounts of moisture may be found on the solution container from water permeating from inside the container. The amount of permeated water is insufficient to affect the solution significantly. If larger amounts of water are found, the container should be checked for tears or leaks.
- Inspect the bag prior to activation. Some opacity of the plastic due to moisture absorption during the sterilization process may be observed. This is normal and does not affect the solution quality or safety. The opacity will diminish gradually. Evaluate the following:
  - If the outlet or additive port protectors are damaged, detached, or not present, discard container as solution path sterility may be impaired.
  - Check to ensure seal between chambers is intact, solutions are contained in separate containers, and the content of the individual chambers is clear, colorless or slightly yellow. Discard if the seal is broken or if the solution is bright yellow or yellowish brown.
  - Check for minute leaks by separately squeezing each chamber. If external leaks or leakage between the chambers are found, discard solution as sterility or stability may be impaired.
  - Lipids and/or additives can be introduced to the container after opening seal between chambers. Because additives may be incompatible, evaluate all additions to the plastic container for compatibility. Activate chambers of bag prior to introduction of additives. Mix thoroughly when additives have been introduced. Supplemental medication may be added with a 19 to 22 gauge needle through the medication port.
  - Calcium and phosphate ratios must be considered. Excess addition of calcium and phosphates, especially in the form of mineral salts, may result in the formation of calcium phosphate precipitates [see Warnings and Precautions (5.1)].
  - Inspect the bag to ensure precipitates have not formed during the mixing or addition of additives. A slight yellow color does not alter the quality and efficacy of this product. If lipid has been added, ensure the emulsion has not separated. Separation of the emulsion can be visibly identified by a yellowish streaking or the accumulation of yellowish droplets in the mixed emulsion. Discard the admixture if any of the above are observed.

2. Important Administration Instructions
- Set the vent to the closed position on a vented intravenous administration set to prevent air embolism.
- Use a dedicated line without any connections to avoid air embolism.
- CLINIMIX is for intravenous infusion only into a central or peripheral vein. The choice of a central or peripheral venous route should depend on the osmolarity of the final infusate. Solutions with osmolality of 900 mOsm/L or greater must be infused through a central catheter [see Warnings and Precautions (5.6)].
2.6 Recommended Dosage in Adults

The recommended daily nutritional requirements for protein and dextrose compared to the amount of nutrition provided by CLINIMIX are shown in Table 1.

As indicated on an individual basis, maintenance vitamins, electrolytes, trace elements and other components (including lipids) should be administered as required to prevent deficiencies and complications from developing.

The maximum infusion rates in adult patients are shown in Table 2.

In addition to meeting protein needs, the administration rate should be 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 blood glucose levels.

### Table 1: Nutritional Comparison – Adult Patients

<table>
<thead>
<tr>
<th>Nutritional Component</th>
<th>Recommended CLINIMIX Nutritional Requirements</th>
<th>Recommended Clinimix Adult Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein (g/kg/day)</td>
<td>0.8 to 1.1 (nitrogen bound)</td>
<td>1.5 to 2.0 (nitrogen bound)</td>
</tr>
<tr>
<td>Amino Acids (g/kg/hour)</td>
<td>0.32 to 0.64 (as required)</td>
<td>0.48 to 0.94 (as required)</td>
</tr>
<tr>
<td>Fluid/Calories (mL/kg/hour)</td>
<td>19 to 40</td>
<td>32 to 50</td>
</tr>
<tr>
<td>Electrolytes (mEq/kg/hour)</td>
<td>as required</td>
<td>as required</td>
</tr>
</tbody>
</table>

### Table 2: Maximum Infusion Rate in Adult Patients

<table>
<thead>
<tr>
<th>Maximum Infusion Rates in Adult Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dextrose (g/kg/hour)</td>
</tr>
<tr>
<td>Amino Acids (g/kg/hour)</td>
</tr>
<tr>
<td>Electrolytes (mEq/kg/hour)</td>
</tr>
</tbody>
</table>

2.7 Dosage Modifications in Patients with Renal Impairment

Before administration, correct severe fluid or electrolyte imbalances. Closely monitor serum electrolyte levels and adjust the volume of CLINIMIX administered as required (see Warning - Precautions (5.10)).

Patients with renal impairment not needing dialysis require 0.6 to 0.8 g of protein/kg/day. Serum electrolyte levels should be closely monitored. Patients on hemodialysis or continuous renal replacement therapy should receive 1.2 to 1.8 g of protein/kg/day up to a maximum of 2.5 g protein/kg/day based on residual renal function and estimated protein losses. The CLINIMIX dosage can be adjusted based on the severity of renal impairment, supplementing protein as indicated. If required, additional amino acids may be added to the CLINIMIX bag or administered separately. Compatibility of additions should be evaluated by a pharmacist and questions may be directed to Baxter.

2.8 Recommended Dosage in Pediatric Patients

The dosage and constant infusion rate of intravenous dextrose must be selected with caution in pediatric patients, particularly neonates and low birth weight infants, because of the increased risk of hyperglycemia/hypoglycemia (see Use in Specific Populations (8.4)). Frequent monitoring of serum glucose concentrations is required when dextrose is prescribed to pediatric patients, particularly newborns and low birth weight infants. The infusion rate and volume should be determined by the consulting physician experienced in pediatric intravenous fluid therapy.

In pediatric patients, CLINIMIX is dosed on the basis of protein provided as amino acids. The recommended dosage, by age group is provided in Tables 3-6. Infusion rates are based on protein and do not take carbohydrates, fluid or electrolytes into consideration. This product does not contain the amino acids cysteine and taurine, considered conditionally essential for neonates and infants. If possible, these amino acids should be added to this product if used in this pediatric population.

### Table 3: Preterm and Term Infants Less than 1 Month of Age

<table>
<thead>
<tr>
<th>Recommended Nutritional Requirements</th>
<th>Recommended Clinical Dosing in Preterm and Term Infants Less than 1 Month of Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein (g/kg/day)</td>
<td>0.27 to 0.54</td>
</tr>
<tr>
<td>Fluid (mL/kg/hour)</td>
<td>17.5 to 35</td>
</tr>
<tr>
<td>Electrolytes (mEq/kg/hour)</td>
<td>as required</td>
</tr>
</tbody>
</table>

### Table 4: Pediatric Patients 1 Month to Less than 1 Year of Age

<table>
<thead>
<tr>
<th>Protein (g/kg/day)</th>
<th>0.32 to 0.64</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluid (mL/kg/hour)</td>
<td>25 to 45</td>
</tr>
<tr>
<td>Electrolytes (mEq/kg/hour)</td>
<td>as required</td>
</tr>
</tbody>
</table>

*Protein is provided as amino acids. When infused intravenously amino acids are metabolized and utilized as the building blocks of protein.

### Table 5: Pediatric Patients 1 Year to Less than 3 Years of Age

<table>
<thead>
<tr>
<th>Protein (g/kg/day)</th>
<th>0.32 to 0.64</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluid (mL/kg/hour)</td>
<td>20 to 40</td>
</tr>
<tr>
<td>Electrolytes (mEq/kg/hour)</td>
<td>as required</td>
</tr>
</tbody>
</table>

*Protein is provided as amino acids. When infused intravenously amino acids are metabolized and utilized as the building blocks of protein.

### Table 6: Pediatric Patients 3 Years to Less than 10 Years of Age

<table>
<thead>
<tr>
<th>Protein (g/kg/day)</th>
<th>0.32 to 0.64</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluid (mL/kg/hour)</td>
<td>15 to 30</td>
</tr>
<tr>
<td>Electrolytes (mEq/kg/hour)</td>
<td>as required</td>
</tr>
</tbody>
</table>

*Protein is provided as amino acids. When infused intravenously amino acids are metabolized and utilized as the building blocks of protein.

### General Considerations

- Lipid emulsion administration should be considered with prolonged use (more than 5 days).
- Monitor levels of serum potassium during therapy. It may be necessary to add potassium when determining the clinically appropriate infusion rate for patients.
- The dosage selection is based only on the recommended protein requirements. The maximum dextrose infusion rates and calorie and fluid requirements must also be considered when determining the clinically appropriate infusion rate for patients.
- CLINIMIX meets the total nutritional requirements for protein and dextrose in stable patients, and can be individualized to meet specific needs with the addition of nutrients.
- Total daily fluid requirements can be met beyond the volume of amino acids solution by supplementing with non-carbohydrate or carbohydrate-containing electrolyte solutions. 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.
- Prior to administration of CLINIMIX correct severe fluid, electrolyte and acid-base disorders.
- Monitor levels of serum potassium during therapy. It may be necessary to add potassium to the CLINIMIX admixture.
- Lipid emulsion administration should be considered with prolonged use (more than 5 days) of CLINIMIX in order to prevent essential fatty acid deficiency (EFA). Serum lipids should be monitored for evidence of EFA in patients maintained on fat-free parenteral nutrition. See prescribing information of lipid emulsion.
- 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.
### 5.2 Hypersensitivity Reactions

Paradoxical reactions and fever, urticaria, angioedema, or other signs of anaphylaxis have been reported. In most cases, the infusion can be continued if the reaction is mild by simply slowing the infusion rate. Severe reactions may require discontinuation of the infusion. If anaphylaxis occurs, discontinue the infusion and begin standard treatment. Patients should be observed until signs and symptoms have resolved.

### 5.3 Renal Function

Dextrose and amino acid solutions are removed primarily by the kidneys. However, increased urine output is not a reliable index of renal function in malnourished patients, and patients should be observed carefully. The risk of hyperkalemia or hyperosmolar hyperglycemic state may increase with larger doses or in patients with impaired renal function.

### 5.4 Hepatic Function

Malnourished patients may have decreased hepatic function.

### 5.5 Hyperglycemia or Hyperosmolar Hyperglycemic State

Hyperglycemia may occur if the rate of dextrose infusion exceeds the capacity of the liver to utilize glucose. In patients with diabetes mellitus, close monitoring of blood glucose levels is necessary to identify and correct this complication.

### 5.6 Pulmonary Function

Patients with pulmonary edema or acidosis due to low cardiac output should be excluded from CLINIMIX therapy. When used in patients who have elevated pulmonary vascular resistance or left ventricular dysfunction, the risk of pulmonary embolism should be considered.

### 5.7 Hepatobiliary Disorders

SCULP therapy, which is contraindicated in patients with fulminating hepatic failure or severe chronic liver disease, should be used with extreme caution in patients with impaired liver function.

### 5.8 Blood Coagulation

When used in patients with liver disease, CLINIMIX should be administered with care. Warfarin is not removed by dialysis.

### 5.9 Infectious Complications

See Section 17.4.2.1. Infections include those caused by Gram-negative and Gram-positive bacteria, as well as fungi, viruses, and yeasts. Use CLINIMIX only in patients where the benefits outweigh the risks. Monitor patients closely for signs of infection.

### 5.10 Other Complications

See Section 17.4.2.2. Non-steroidal anti-inflammatory drugs may inhibit the anticoagulant effects of warfarin.

### 5.11 Bone Disease

See Section 17.4.2.3. Patients on long-term CLINIMIX therapy may develop osteoporosis, which may require treatment with bisphosphonates or other osteoporosis medications.

### 5.12 Cardiac Tissue

See Section 17.4.2.4. Long-term dextrose and amino acid therapy may increase the risk of cardiac arrhythmias.

### 5.13 Skin Complications

See Section 17.4.2.5. Patients on long-term CLINIMIX therapy may develop skin complications, such as pruritus and rash.

### 5.14 Other

See Section 17.4.2.6. Other complications may include those related to the infusion route or site, such as local irritation, phlebitis, or infection.
Monitor liver function parameters and ammonia levels. Patients developing signs of hepatic failure should be assessed early by a clinician knowledgeable in renal disease in order to determine the appropriate CLINIMIX dosage and other treatment options.

5.9 Risk of Parenteral Nutrition Associated Liver Disease

Parenteral Nutrition Associated Liver Disease (PNALD) has been reported in patients who receive parenteral nutrition for extended periods of time, especially preterm infants, and can present as cholestasis or steatohepatitis. The exact etiology is unknown and is likely multifactorial. If CLINIMIX treated patients develop liver test abnormalities consider discontinuation or dosage reduction.

5.10 Electrolyte Imbalance and Fluid Overload

Patients with renal impairment, such as pre-renal azotemia, renal obstruction, and pre-renal lopping nephropathy may be at increased risk of electrolyte and fluid volume imbalance. Patients with cardiorenal disease due to heart insufficiency or systemic dysfunctions are susceptible to excess fluid accumulation. Use CLINIMIX with caution in patients with cardiac insufficiency or renal impairment. CLINIMIX dosage may require adjustment with specific attention to fluid, protein, and electrolyte control in these patients. Monitor renal function parameters. Patients developing signs of renal impairment should be assessed early by a clinician knowledgeable in renal disease in order to determine the appropriate CLINIMIX dosage and other treatment options.

5.11 Monitoring/Laboratory Tests

Monitor fluid and electrolyte status, serum osmolality, blood glucose, liver and kidney function, blood count and coagulation parameters throughout treatment. Patients receiving CLINIMIX should be monitored frequently and their electrolyte requirements individualized.

6 ADVERSE REACTIONS

The following serious adverse reactions are discussed in greater detail in other sections of the prescribing information.

• Pulmonary embolism due to pulmonary vascular precipitates [see Warnings and Precautions (5.1)].
• Hypersensitivity reactions [see Warnings and Precautions (5.2)].
• Risk of Infections [see Warnings and Precautions (5.3)].
• Refeeding syndrome [see Warnings and Precautions (5.4)].
• Hypoglycemia or hyperosmolar hyperglycemic state [see Warnings and Precautions (5.5)].
• Venous damage and thrombosis [see Warnings and Precautions (5.6)].
• Hepatobiliary disorders [see Warnings and Precautions (5.7)].
• Parenteral Nutrition Associated Liver Disease [see Warnings and Precautions (5.8)].
• Electrolyte imbalance and fluid overload [see Warnings and Precautions (5.9)].

The following adverse reactions from voluntary reports or clinical studies have been reported with CLINIMIX. Because many of these reactions were reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

• Diuresis
• Extravasation
• Glossectomy
• Hyperglycemia
• Hypersomolar coma

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no adequate or well-controlled studies in pregnant women with CLINIMIX. Additional, animal reproduction studies have not been conducted with amino acids and electrolytes and dextrose. It is not known whether CLINIMIX can cause fetal harm when administered to a pregnant woman.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. However, the estimated background risk in the United States general population of major birth defects is 2 to 4% and of miscarriage is 15 to 20% of clinically recognized pregnancies.

Clinical Considerations

Disease-Associated Maternal and/or Embryo-Fetal Risk

Based on clinical practice guidelines, prenatal nutrition should be considered in cases of severe maternal malnutrition where nutritional requirements cannot be fulfilled by the enteral route due to the risks associated with severe maternal malnutrition, such as preterm delivery, low birth weight, intrauterine growth restriction, congenital malformations and perinatal mortality.

8.2 Lactation

Risk Summary

It is not known whether CLINIMIX is present in human milk. There are no data on the effects of CLINIMIX on the breastfed infant or on milk production. The development and health benefits of breastfeeding should be considered along with the mother’s clinical need for CLINIMIX and any potential adverse effects on the breastfed child from CLINIMIX or from the underlying maternal condition.

8.4 Pediatric Use

Safety and effectiveness of CLINIMIX in pediatric patients have not been established by adequate and well-controlled studies. Use of dextrose, amino acid infusions and electrolytes in pediatric patients is based on clinical practice [see Dosage and Administration (2.8)].

Newborns, especially those born premature and with low birth weight, are at increased risk of developing hypo- or hyperglycemia and therefore need close monitoring during treatment with intravenous glucose solutions to ensure adequate glycemic control in order to avoid potential long term adverse effects. Hyperglycemia in the newborn can cause prolonged hyperglycemia, and then hypoglycemia followed by hypoglycemia has been associated with intraventricular hemorrhage, late onset bacterial and fungal infection, retinopathy of prematurity, necrotizing enterocolitis, bronchopulmonary dysplasia, prolonged length of hospital stay, and death. Plasma electrolyte concentrations should be closely monitored in the pediatric population as this population may have impaired ability to regulate fluids and electrolytes. Because of immature renal function, preterm infants receiving prolonged treatment with CLINIMIX may be at risk of aluminum toxicity [see Warnings and Precautions (5.9)].

Patients, including pediatric patients, may be at risk for Parenteral Nutrition Associated Liver Disease (PNALD) [see Warnings and Precautions (5.8)].

Hyperammonemia is of special significance in infants (birth to two years). This reaction appears to be related to a deficiency of the urea cycle amino acids of genetic or product origin. It is essential that blood ammonia be measured frequently in infants [see Warnings and Precautions (5.9)].

8.5 Geriatric Use

Clinical studies of CLINIMIX did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from other younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients.

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

10 OVERDOSAGE

An increased infusion rate of CLINIMIX can cause hyperglycemia, hyperosmolarity, and adverse effects on water and electrolyte balance [see Warnings and Precautions (5.5, 5.10)].

Severe hyperglycemia and severe dilutional hypotension, and their complications, can be fatal.

Discontinue infusion and institute appropriate corrective measures in the event of overhydration or solute overload during therapy, with particular attention to respiratory and cardiovascular systems.

For current information on the management of poisoning or overdosage, contact the National Poison Control Center at 1-800-222-1222 or www.poisong.org.

11 DESCRIPTION

CLINIMIX sulfite-free (amino acids in dextrose) injection for intravenous use consists of sterile, nonpyrogenic, hypertonic solutions in a dual chamber container. The outlet port container contains essential and nonessential amino acids. The formulas for the individual amino acids found in CLINIMIX sulfite-free (Amino Acid in Dextrose) Injections are provided in Table 8.

The injection port chamber contains dextrose. Dextrose, USP, is chemically designated D-glucose, monohydrate (C6H12O6·H2O) and has the following structure:

\[
\text{HO-CH(\text{OH})_2} \rightarrow \text{HO-CH(\text{OH})_2} + \text{H}_2\text{O}
\]

Dextrose is derived from corn. See Table 7 for composition, pH, osmolarity, ionic concentration and caloric content of the admixed product [see Dosage Forms and Strengths (3)].

The dual chamber container is a lipid-compatible plastic container (PL 2401 Plastic). CLINIMIX contains no more than 25 mcg of aluminum.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

CLINIMIX is used as a supplement of nutrition in patients, providing macronutrients (amino acids and dextrose) parenterally.

The amino acids provide the structural units that make up proteins and are used to synthesize proteins and other biomolecules or are oxidized to urea and carbon dioxide as a source of energy.

The administered dextrose is oxidized to carbon dioxide and water, yielding energy.

12.3 Pharmacokinetics

The disposition of infused amino acids and dextrose, are essentially the same as those absorbed from ordinary food.

15 REFERENCES


16 HOW SUPPLIED/STORAGE AND HANDLING

CLINIMIX (amino acids in dextrose) injection (sulfite-free) is available in 1000 mL and 2000mL volumes (see Table 9).
Table 9: CLINIMIX Formulations

<table>
<thead>
<tr>
<th>CLINIMIX</th>
<th>Code</th>
<th>NDC Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.75% Amino Acid in 5% Dextrose</td>
<td>Code 2B7705</td>
<td>NDC 0338-1152-03</td>
</tr>
<tr>
<td>2000 mL Code and NDC Number</td>
<td>Code 2B7701</td>
<td>NDC 0338-1150-04</td>
</tr>
<tr>
<td>2.75% Amino Acid in 5% Dextrose</td>
<td>Code 2B7706</td>
<td>NDC 0338-1153-03</td>
</tr>
<tr>
<td>4.25% Amino Acid in 5% Dextrose</td>
<td>Code 2B7707</td>
<td>NDC 0338-1154-03</td>
</tr>
<tr>
<td>4.25% Amino Acid in 5% Dextrose</td>
<td>Code 2B7708</td>
<td>NDC 0338-1155-03</td>
</tr>
<tr>
<td>4.25% Amino Acid in 10% Dextrose</td>
<td>Code 2B7709</td>
<td>NDC 0338-1156-03</td>
</tr>
<tr>
<td>4.25% Amino Acid in 20% Dextrose</td>
<td>Code 2B7710</td>
<td>NDC 0338-1157-03</td>
</tr>
<tr>
<td>4.25% Amino Acid in 25% Dextrose</td>
<td>Code 2B7711</td>
<td>NDC 0338-1158-03</td>
</tr>
</tbody>
</table>

Minimize exposure of CLINIMIX to heat and avoid excessive heat. Protect from freezing. Store CLINIMIX at room temperature (25°C/77°F) (may briefly store at up to 40°C/104°F). Refrigerated storage is limited to 9 days once the protective foil overwrap has been opened. Do not use if the protective foil overwrap has been previously opened or damaged. For storage of admixed solutions see Dosage and Administration (2.3, 2.4).

17 PATIENT COUNSELING INFORMATION

Inform patients, caregivers, or home healthcare providers of the following risks of CLINIMIX:

- Pulmonary embolism due to pulmonary vascular precipitates [see Warnings and Precautions (5.1)]
- Hypersensitivity reactions [see Warnings and Precautions (5.2)]
- Risk of infections [see Warnings and Precautions (5.3)]
- Refeeding syndrome [see Warnings and Precautions (5.4)]
- Hyperglycemia or hyperosmolar hyperglycemic state [see Warnings and Precautions (5.5)]
- Vein damage and thrombosis [see Warnings and Precautions (5.6)]
- Hepatobiliary disorders [see Warnings and Precautions (5.7)]
- Aluminum toxicity [see Warnings and Precautions (5.8)]
- Parenteral Nutrition Associated Liver Disease (PNALD) [see Warnings and Precautions (5.9)]
- Electrolyte imbalance and fluid overload [see Warnings and Precautions (5.10)]

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Deerfield, IL 60015 USA
Printed in USA

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FULL PRESCRIBING INFORMATION: CONTENTS*  
1 INDICATIONS AND USAGE  
2 DOSAGE AND ADMINISTRATION  
3 DOSAGE FORMS AND STRENGTHS  
4 CONTRAINDICATIONS  
5 WARNINGS AND PRECAUTIONS  
6 ADVERSE REACTIONS  
7 DRUG INTERACTIONS  
8 USE IN SPECIFIC POPULATIONS  
10 OVERDOSAGE  
11 DESCRIPTION  
12 CLINICAL PHARMACOLOGY  
13 REFERENCES  
14 HOW SUPPLIED/STORAGE AND HANDLING  
17 PATIENT COUNSELING INFORMATION  
*Sections or subsections omitted from the full prescribing information are not listed.
account the dose being administered, the daily volume intake, and the duration of the infusion.

2.6 Recommended Dosage in Adults

The recommended daily nutritional requirements for protein and dextrose compare to the amount of nutrition provided by CLINIMIX E are shown in Table 1. As indicated on an individual basis, maintenance vitamins, additional electrolytes, trace elements and other components (including lipids) should be administered as required to prevent deficiencies and complications from developing.

The maximum infusion rates in adult patients are shown in Table 2. In addition to meeting protein needs, the administration rate should be governed, especially during the first few day 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 blood glucose levels.

Table 1: Nutritional Comparison – Adult Patients

<table>
<thead>
<tr>
<th>Requirement</th>
<th>Recommended Nutritional Requirements</th>
<th>Recommended Clinical E Adult Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fluid (mL/kg/day)</strong></td>
<td>2.5</td>
<td>2.5</td>
</tr>
<tr>
<td><strong>Protein (g/kg/day)</strong></td>
<td>0.8</td>
<td>0.8</td>
</tr>
<tr>
<td><strong>Carbohydrate (g/kg/day)</strong></td>
<td>3.5</td>
<td>3.5</td>
</tr>
<tr>
<td><strong>Electrolyte</strong></td>
<td>108</td>
<td>108</td>
</tr>
</tbody>
</table>

Table 2: Maximum Infusion Rate in Adult Patients

<table>
<thead>
<tr>
<th>Maximum Infusion Rate (mL/kg/hr)</th>
<th>Adult Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.75</td>
</tr>
<tr>
<td>2</td>
<td>2.5</td>
</tr>
<tr>
<td>3</td>
<td>3.25</td>
</tr>
<tr>
<td>4</td>
<td>4.0</td>
</tr>
</tbody>
</table>

2.7 Dosage Modifications in Patients with Renal Impairment

Prior to administration, correct severe fluid or electrolyte imbalances. Close monitor serum electrolyte levels and adjust the volume of CLINIMIX E administered as required [see Warnings and Precautions (5.11)].

Patients with renal impairment not needing dialysis should receive 0.6 to 0.8 g of protein/kg/day. Serum electrolyte levels should be closely monitored. Patients on hemodialysis or continuous renal replacement therapy should receive 1.2 to 1.8 g of protein/kg/day up to a maximum of 2.5 g of protein/kg/day based on nutritional status and estimated protein losses. The CLINIMIX E dosage can be adjusted based on the severity of renal impairment, supplementing protein as indicated. If required, additional amino acids may be added to the CLINIMIX E bag or infused separately. Compatibility of additions should be evaluated by a pharmacist and any additions be directed to Baxter.

2.8 Recommended Dosage in Pediatric Patients

The dosage and constant infusion rate of intravenous dextrose must be selected with caution in pediatric patients, particularly neonates and low weight infants, because of the increased risk of hypoglycemia/hyperglycemia [see Use in Specific Populations (8.4)]. Frequent monitoring of serum glucose concentrations is required when dextrose is prescribed to pediatric patients, particularly neonates and low birth weight infants. The infusion rate and volume should be determined by the consulting physician experienced in pediatric intravenous fluid therapy.

In pediatric patients, CLINIMIX E is dosed on the basis of protein provided as amino acids. The recommended dosage, by age group is provided in Table 3. Infusion rates are based on protein and do not take carbohydrates, fluid or electrolytes into consideration. This product does not contain the amino acids cysteine and taurine, considered conditional-essential for neonates and infants. If possible, these amino acids should be added to this product if used in this pediatric population.

Table 3: Preterm and Term Infants Less than 1 Month of Age

<table>
<thead>
<tr>
<th>Requirement</th>
<th>Recommended Nutritional Requirements</th>
<th>Recommended Clinical E Dosage in Preterm and Term Infants Less than 1 Month of Age</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fluid (mL/kg/day)</strong></td>
<td>3 to 4.5</td>
<td>3 to 4.5</td>
</tr>
<tr>
<td><strong>Protein (g/kg/day)</strong></td>
<td>1.45 to 2</td>
<td>1.45 to 2</td>
</tr>
<tr>
<td><strong>Electrolyte</strong></td>
<td>7.2 to 10.8</td>
<td>7.2 to 10.8</td>
</tr>
</tbody>
</table>

Table 4: Pediatric Patients 1 Month to Less than 1 Year of Age

<table>
<thead>
<tr>
<th>Requirement</th>
<th>Recommended Nutritional Requirements</th>
<th>Recommended Clinical E Dosage in Pediatric Patients 1 Month to Less than 1 Year of Age</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fluid (mL/kg/day)</strong></td>
<td>2.5 to 3</td>
<td>2.5 to 3</td>
</tr>
<tr>
<td><strong>Protein (g/kg/day)</strong></td>
<td>1.0 to 1.4</td>
<td>1.0 to 1.4</td>
</tr>
<tr>
<td><strong>Electrolyte</strong></td>
<td>7 to 10</td>
<td>7 to 10</td>
</tr>
</tbody>
</table>

*Protein is provided as amino acids. When infused intravenously amino acids are metabolized and utilized as the building blocks of protein.
Table 5: Pediatric Patients 1 Year to Less than 11 Years of Age

<table>
<thead>
<tr>
<th>Fluid</th>
<th>Electrolyte Profile</th>
<th>Calcium Chloride Dihydrate, USP</th>
<th>Magnesium Chloride, USP</th>
<th>Dibasic Potassium Phosphate, USP</th>
<th>Tyrosine</th>
<th>Serine</th>
<th>Glycine</th>
<th>Alanine</th>
<th>Tryptophan</th>
<th>Methionine</th>
<th>Lysine (added as the hydrochloride salt)</th>
<th>Dextrose Hydrous, USP (g/100 mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.5 to 3</td>
<td>0.8 to 1.5</td>
<td>1.07 to 3.5</td>
<td>0.31 to 0.60</td>
<td>0.32</td>
<td>0.35</td>
<td>0.47</td>
<td>0.50</td>
<td>0.60</td>
<td>0.70</td>
<td>0.80</td>
<td>0.90</td>
<td>1.00</td>
</tr>
<tr>
<td>1.5 to 3</td>
<td>0.8 to 1.5</td>
<td>1.07 to 3.5</td>
<td>0.31 to 0.60</td>
<td>0.32</td>
<td>0.35</td>
<td>0.47</td>
<td>0.50</td>
<td>0.60</td>
<td>0.70</td>
<td>0.80</td>
<td>0.90</td>
<td>1.00</td>
</tr>
<tr>
<td>1 to 2</td>
<td>1.2 to 2.3</td>
<td>1.6 to 3.4</td>
<td>0.44 to 0.66</td>
<td>0.60</td>
<td>0.80</td>
<td>0.80</td>
<td>0.80</td>
<td>0.80</td>
<td>0.80</td>
<td>0.80</td>
<td>0.80</td>
<td>0.80</td>
</tr>
<tr>
<td>17 to 31</td>
<td>570</td>
<td>320</td>
<td>120</td>
<td>30</td>
<td>0.3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2. Discontinuation of CLINIMIX

To reduce the risk of hypoglycemia after discontinuation, a gradual decrease in flow rate in the last hour of infusion should be considered.

3. DOSAGE FORMS AND STRENGTHS

CLINIMIX E injection is available in 1000 mL and 2000 mL dual chamber bags. The individual chambers contain essential and nonessential amino acids with electrolytes and dextrose with calcium. Table 7 describes the individual components of CLINIMIX E.

Table 7 Ingredients per 100mL of CLINIMIX E

<table>
<thead>
<tr>
<th>Strength of CLINIMIX E</th>
<th>CALCIMIX E 5% Lysine/sulfate (0.25% Amino Acid in 5% Dextrose)</th>
<th>CALMIX E 2.5% Lysine/sulfate (0.75% Amino Acid in 2.5% Dextrose)</th>
<th>CALMIX E 1.25% Lysine/sulfate (0.375% Amino Acid in 1.25% Dextrose)</th>
<th>CALMIX E 1% Lysine/sulfate (0.25% Amino Acid in 1% Dextrose)</th>
<th>CALMIX E 0.5% Lysine/sulfate (0.125% Amino Acid in 0.5% Dextrose)</th>
<th>CALMIX E 0.25% Lysine/sulfate (0.0625% Amino Acid in 0.25% Dextrose)</th>
<th>CALMIX E 0.2% Lysine/sulfate (0.04% Amino Acid in 0.2% Dextrose)</th>
<th>CALMIX E 0.1% Lysine/sulfate (0.02% Amino Acid in 0.1% Dextrose)</th>
<th>CALMIX E 0.05% Lysine/sulfate (0.01% Amino Acid in 0.05% Dextrose)</th>
<th>CALMIX E 0.025% Lysine/sulfate (0.005% Amino Acid in 0.025% Dextrose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infusion Rate Range (mL/hg)</td>
<td>0.8 to 1.5</td>
<td>1.07 to 3.5</td>
<td>0.31 to 0.60</td>
<td>0.32</td>
<td>0.35</td>
<td>0.47</td>
<td>0.50</td>
<td>0.60</td>
<td>0.70</td>
<td>0.80</td>
</tr>
</tbody>
</table>

4. CONTRAINDICATIONS

The use of CLINIMIX E is contraindicated in:

- Neonates (less than 28 days of age) receiving concomitant treatment with ceftriaxone, even if separate infusion lines are used, due to the risk of fatal ceftriaxone calcium salt precipitation in the neonate’s bloodstream (see Warnings and Precautions (5.2), Use in Specific Populations (8.4)).
- Patients with known hypersensitivity to one or more amino acids or dextrose (see Warnings and Precautions (5.3)).
- Patients with inborn errors of amino acid metabolism due to risk of severe metabolic and neurologic complications.
- Patients with pulmonary edema or acidosis due to low cardiac output.

5. WARNINGS AND PRECAUTIONS

5.1 Pulmonary Embolism due to Pulmonary Vascular Precipitates

Pulmonary vascular precipitates causing pulmonary vascular emboli and pulmonary dis- tress have been reported in patients receiving parenteral nutrition. In some cases, fatal outcomes due to pulmonary embolism have occurred. Patients, especially those with hypo- phosphatemia, may require the addition of phosphate. To prevent hypocalcemia, supplementation should always accompany phosphate administration. Excessive addition of calcium and phosphate increases the risk of the formation of calcium phosphate precipitates. Precipitates have been reported even in the absence of phosphate salt in the solution. Precipitation following passage through an in-line filter and suspected in vivo precipitation formation has also been reported. If signs of pulmonary distress occur, stop the infusion and initiate a medical evaluation. In addition to inspection of the solution (see Dosage and Administration (2.1, 2.2, 2.3, 2.4)), the infusion set and catheter should also periodically be checked for precipitates.

5.2 Precipitation with Ceftriaxone

Precipitation of ceftriaxone-calcium can occur when ceftriaxone is mixed with calcium-con- taining parenteral nutrition solutions, such as CLINIMIX E, in the same intravenous admin- istration line. Do not administer ceftriaxone simultaneously with CLINIMIX E via a Y-site. Deaths have occurred in neonates (less than 28 days of age) who received concomitant intra- venous calcium-containing solutions with ceftriaxone resulting from calcium-ceftriaxone precipitates in the lungs and kidneys, even when separate infusion lines were used. CLINIMIX E is contraindicated in neonates receiving ceftriaxone (see Contraindications (4.6), Use in Specific Populations (8.4)).

In patients older than 28 days (including adults), ceftriaxone and CLINIMIX E may be ad- ministered concurrently if the infusion lines are thoroughly flushed between infusions with a compatible fluid.

5.3 Hypersensitivity Reactions

Hypersensitivity reaction reactions including anaphylaxis have been reported with CLINI- MIX E. Stop infusion immediately and treat patient accordingly if any signs or symptoms of a hypersensitivity reaction develop. Signs or symptoms may include: hypotension, hyperther- mia, peripheral cyanosis, tachycardia, dyspnea, vomiting, nausea, urticaria, rash, pruritus, erythema, hypotension, pyrexia, and chills.

5.4 Risk of Infections

Patients who require parenteral nutrition are at high risk of infections because the nutritional components of these solutions can support microbial growth. Infection and sepsis may also occur as a result of the use of intravenous catheters to administer parenteral nutrition. The risk of infection is increased in patients with malnutrition-associated immunosuppression. Hypoglycemia exacerbated by dextrose infusion, long-term use and poor maintenance of intravenous catheters, or immunosuppressive effects of other concomitant conditions, drugs, or other components of the parenteral formulation (e.g., lipid emulsion). To decrease the risk of infection, ensure aseptic technique in catheter placement and main- tenance, as well as aseptic technique in the preparation and administration of the nutritional formula.

Monitor for signs and symptoms (including fever and chills) of early infections, including...
8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no adequate or well-controlled studies in pregnant women with CLINIMIX E. Additionally, animal reproduction studies have not been conducted with amino acids and electrolytes and dextrose. It is not known whether CLINIMIX E can cause fetal harm when administered to a pregnant woman.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. However, the estimated background risk in the U.S. general population of major birth defects is 2% to 4% and of miscarriage is 15% to 20% of clinically recognized pregnancies.

Clinical Considerations

- Disease-Associated Maternal and/or Embryo-Fetal Risk

Based on clinical practice guidelines, parenteral nutrition should be considered in cases of severe maternal malnutrition where nutritional requirements cannot be fulfilled by the enteral route because of the risks to the fetus associated with severe maternal malnutrition, such as preterm delivery, low birth weight, intrauterine growth restriction, congenital malformations and perinatal mortality.

8.2 Lactation

Risk Summary

It is not known whether CLINIMIX E is present in human milk. There are no data on the effects of CLINIMIX E on the breastfed infant or on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for CLINIMIX E and any potential adverse effects on the breastfed child from CLINIMIX E or from the underlying maternal condition.

8.4 Pediatric Use

Safety and effectiveness of CLINIMIX E in pediatric patients have not been established by adequate and well-controlled studies. Use of dextrose, amino acid infusions and electrolytes in pediatric patients is based on clinical practice (see Dosage and Administration (2.8)).

Deaths have occurred in neonates (less than 28 days of age) who received concomitant intravenous calcium-containing solutions with ceftriaxone resulting from calcium-ceftriaxone precipitates. To minimize the risk of such kidney damage, even when separate infusion lines were used, CLINIMIX E is contraindicated in neonates receiving ceftriaxone (see Contraindications (4), Warnings and Precautions (5.2)).

Newborns, especially those born premature and with low birth weight, are at increased risk of developing hypoxi—or hyperglycemia and therefore need close monitoring during treatment with intravenous glucose solutions to ensure adequate glycemic control in order to avoid potential long term adverse effects. Hyperglycemia in the newborn can cause postnatal hyperammonemia, which can present as cholestasis or steatohepatitis. The exact etiology is unknown and is likely multifactorial. If CLINIMIX E treated patients develop liver test abnormalities, consider discontinuation or dose reduction.

11 DESCRIPTION

Table 8: Formulas for Amino Acids

<table>
<thead>
<tr>
<th>Amino Acid</th>
<th>Formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alanine</td>
<td>C_3H_7NO_2</td>
</tr>
<tr>
<td>Arginine</td>
<td>C_6H_14N_3O_2</td>
</tr>
<tr>
<td>Aspartic acid</td>
<td>C_4H_7NO_4</td>
</tr>
<tr>
<td>Cysteine</td>
<td>C_3H_7NO_3S</td>
</tr>
<tr>
<td>Glutamic acid</td>
<td>C_5H_9NO_4</td>
</tr>
<tr>
<td>Glutamine</td>
<td>C_5H_10N_3O_2</td>
</tr>
<tr>
<td>Glycine</td>
<td>C_2H_5NO</td>
</tr>
<tr>
<td>Histidine</td>
<td>C_6H_11O_2N_2</td>
</tr>
<tr>
<td>Isoleucine</td>
<td>C_6H_13NO_2</td>
</tr>
<tr>
<td>Leucine</td>
<td>C_6H_14NO_2</td>
</tr>
<tr>
<td>Lysine</td>
<td>C_6H_14N_2O_2</td>
</tr>
<tr>
<td>Methionine</td>
<td>C_5H_11NO_2S</td>
</tr>
<tr>
<td>Phenylalanine</td>
<td>C_9H_11NO_2</td>
</tr>
<tr>
<td>Proline</td>
<td>C_5H_9NO_2</td>
</tr>
<tr>
<td>Serine</td>
<td>C_3H_7NO</td>
</tr>
<tr>
<td>Threonine</td>
<td>C_3H_7NO_2</td>
</tr>
<tr>
<td>Tyrosine</td>
<td>C_9H_11NO_2</td>
</tr>
<tr>
<td>Valine</td>
<td>C_6H_14NO_2</td>
</tr>
</tbody>
</table>

Essential Amino Acids

- Alanine
- Aspartic acid
- Cysteine
- Glutamic acid
- Histidine
- Isoleucine
- Leucine
- Lysine
- Methionine
- Phenylalanine
- Proline
- Serine
- Threonine
- Tyrosine
- Valine

Non-Essential Amino Acids

- Arginine
- Glutamine
- Glycine
- Histidine
- Proline
- Serine
- Threonine
- Tyrosine
- Valine

Sodium Chloride

| Sodium Chloride | NaCl |

Magnesium Chloride

| Magnesium Chloride | MgCl_2 |

Sulfite

| Sulfite | C_2H_3O_2S |

Sulfate

| Sulfate | C_2H_3O_2S |

Table: Formulas for Amino Acids

<table>
<thead>
<tr>
<th>Amino Acid</th>
<th>Formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alanine</td>
<td>C_3H_7NO_2</td>
</tr>
<tr>
<td>Arginine</td>
<td>C_6H_14N_3O_2</td>
</tr>
<tr>
<td>Aspartic acid</td>
<td>C_4H_7NO_4</td>
</tr>
<tr>
<td>Cysteine</td>
<td>C_3H_7NO_3S</td>
</tr>
<tr>
<td>Glutamic acid</td>
<td>C_5H_9NO_4</td>
</tr>
<tr>
<td>Glutamine</td>
<td>C_5H_10N_3O_2</td>
</tr>
<tr>
<td>Glycine</td>
<td>C_2H_5NO</td>
</tr>
<tr>
<td>Histidine</td>
<td>C_6H_11O_2N_2</td>
</tr>
<tr>
<td>Isoleucine</td>
<td>C_6H_13NO_2</td>
</tr>
<tr>
<td>Leucine</td>
<td>C_6H_14NO_2</td>
</tr>
<tr>
<td>Lysine</td>
<td>C_6H_14N_2O_2</td>
</tr>
<tr>
<td>Methionine</td>
<td>C_5H_11NO_2S</td>
</tr>
<tr>
<td>Phenylalanine</td>
<td>C_9H_11NO_2</td>
</tr>
<tr>
<td>Proline</td>
<td>C_5H_9NO_2</td>
</tr>
<tr>
<td>Serine</td>
<td>C_3H_7NO</td>
</tr>
<tr>
<td>Threonine</td>
<td>C_3H_7NO_2</td>
</tr>
<tr>
<td>Tyrosine</td>
<td>C_9H_11NO_2</td>
</tr>
<tr>
<td>Valine</td>
<td>C_6H_14NO_2</td>
</tr>
</tbody>
</table>

Essential Amino Acids

- Alanine
- Aspartic acid
- Cysteine
- Glutamic acid
- Histidine
- Isoleucine
- Leucine
- Lysine
- Methionine
- Phenylalanine
- Proline
- Serine
- Threonine
- Tyrosine
- Valine

Non-Essential Amino Acids

- Arginine
- Glutamine
- Glycine
- Histidine
- Proline
- Serine
- Threonine
- Tyrosine
- Valine

Sodium Chloride

| Sodium Chloride | NaCl |

Magnesium Chloride

| Magnesium Chloride | MgCl_2 |

Sulfite

| Sulfite | C_2H_3O_2S |

Sulfate

| Sulfate | C_2H_3O_2S |
The injection port chamber contains dextrose with calcium. The formula for Calcium Chloride is: C2H2O • H2O. Dextrose, USP, is chemically designated D-glucose, monohydrate (C6H12O6 • H2O) and has the following structure:

![Dextrose Structure](image)

Dextrose is derived from corn. See Table 7 for composition, pH, osmolality, ionic concentration and caloric content of the admixed product (see Dosage Forms and Strengths).

The dual chamber container is a lipid-compatible plastic container (PL 2401 Plastic).

12.3 Pharmacokinetics

The disposition of infused amino acids, dextrose, and electrolytes are essentially the same as those absorbed from food.

15 REFERENCES


16 HOW SUPPLIED/STORAGE AND HANDLING

CLINIMIX E (amino acids with electrolytes in dextrose with calcium) injection (sulfite-free) is available in 1000 mL and 2000 mL volumes (See Table 9).

Minimize exposure of CLINIMIX E to heat and avoid excessive heat. Protect from freezing.

Store CLINIMIX E at room temperature (25°C/77°F) (may briefly store at up to 40°C/104°F). Refrigerated storage is limited to 9 days once the protective foil overwrap has been opened. Do not use if the protective foil overwrap has been previously opened or damaged.

For storage of admixed solutions see Dosage and Administration (2.3, 2.4).

17 PATIENT COUNSELING INFORMATION

Inform patients, caregivers, or home healthcare providers of the following risks of CLINIMIX E:

- Pulmonary embolism due to pulmonary vascular precipitates (see Warnings and Precautions (5.1))
- Death in neonates due to calcium-ceftriaxone precipitates (see Warnings and Precautions (5.9))
- Hypersensitivity reactions (see Warnings and Precautions (5.10))
- Vein damage and thrombosis (see Warnings and Precautions (5.7))
- Hepatobiliary disorders (see Warnings and Precautions (5.8))
- Aluminum toxicity (see Warnings and Precautions (5.9))
- Parenteral Nutrition Associated Liver Disease (PNALD) (see Warnings and Precautions (5.10))
- Electrolyte imbalance and fluid overload (see Warnings and Precautions (5.11))

Table 9: CLINIMIXE Formulations

<table>
<thead>
<tr>
<th>After mixing, the product represents</th>
<th>1000 mL Code and NDC Number</th>
<th>2000 mL Code and NDC Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>CLINIMIX E 2.75% sulfite-free (2.75% Amino Acid with Electrolytes in 5% Dextrose with Calcium) Injection</td>
<td>Code 037714 NDC 0338-1105-04</td>
<td>Code 037714 NDC 0338-1105-04</td>
</tr>
<tr>
<td>CLINIMIX E 2.75% sulfite-free (2.75% Amino Acid with Electrolytes in 10% Dextrose with Calcium) Injection</td>
<td>Code 037717 NDC 0338-1105-04</td>
<td>Code 037717 NDC 0338-1105-04</td>
</tr>
<tr>
<td>CLINIMIX E 4.25% sulfite-free (4.25% Amino Acid with Electrolytes in 5% Dextrose with Calcium) Injection</td>
<td>Code 037717 NDC 0338-1105-04</td>
<td>Code 037717 NDC 0338-1105-04</td>
</tr>
<tr>
<td>CLINIMIX E 4.25% sulfite-free (4.25% Amino Acid with Electrolytes in 10% Dextrose with Calcium) Injection</td>
<td>Code 037717 NDC 0338-1105-04</td>
<td>Code 037717 NDC 0338-1105-04</td>
</tr>
<tr>
<td>CLINIMIX E 4.25% sulfite-free (4.25% Amino Acid with Electrolytes in 15% Dextrose with Calcium) Injection</td>
<td>Code 037717 NDC 0338-1105-04</td>
<td>Code 037717 NDC 0338-1105-04</td>
</tr>
<tr>
<td>CLINIMIX E 4.25% sulfite-free (4.25% Amino Acid with Electrolytes in 20% Dextrose with Calcium) Injection</td>
<td>Code 037717 NDC 0338-1105-04</td>
<td>Code 037717 NDC 0338-1105-04</td>
</tr>
<tr>
<td>CLINIMIX E 4.25% sulfite-free (4.25% Amino Acid with Electrolytes in 25% Dextrose with Calcium) Injection</td>
<td>Code 037717 NDC 0338-1105-04</td>
<td>Code 037717 NDC 0338-1205-04</td>
</tr>
<tr>
<td>CLINIMIX E 4.25% sulfite-free (4.25% Amino Acid with Electrolytes in 30% Dextrose with Calcium) Injection</td>
<td>Code 037717 NDC 0338-1105-04</td>
<td>Code 037717 NDC 0338-1105-04</td>
</tr>
<tr>
<td>CLINIMIX E 5/25 sulfite-free (5% Amino Acid with Electrolytes in 10% Dextrose with Calcium) Injection</td>
<td>Code 037721 NDC 0338-1105-04</td>
<td>Code 037721 NDC 0338-1105-04</td>
</tr>
<tr>
<td>CLINIMIX E 5/20 sulfite-free (5% Amino Acid with Electrolytes in 15% Dextrose with Calcium) Injection</td>
<td>Code 037721 NDC 0338-1105-04</td>
<td>Code 037721 NDC 0338-1105-04</td>
</tr>
<tr>
<td>CLINIMIX E 5/15 sulfite-free (5% Amino Acid with Electrolytes in 20% Dextrose with Calcium) Injection</td>
<td>Code 037721 NDC 0338-1105-04</td>
<td>Code 037721 NDC 0338-1105-04</td>
</tr>
<tr>
<td>CLINIMIX E 5/10 sulfite-free (5% Amino Acid with Electrolytes in 25% Dextrose with Calcium) Injection</td>
<td>Code 037721 NDC 0338-1105-04</td>
<td>Code 037721 NDC 0338-1105-04</td>
</tr>
</tbody>
</table>

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