

PRODUCT MONOGRAPH
INCLUDING PATIENT MEDICATION INFORMATION

OLIMEL 3.3% E

Amino acids **WITH** electrolytes, dextrose, lipids
Injectable Emulsion
3.3% w/v & 0.7% w/v, 11.5% w/v, 4% w/v

OLIMEL 4.4% E

Amino acids **WITH** electrolytes, dextrose, lipids
Injectable Emulsion
4.4% w/v & 0.7% w/v, 14% w/v, 4% w/v

OLIMEL 5.7% E

Amino acids **WITH** electrolytes, dextrose, lipids
Injectable Emulsion
5.7% w/v & 0.7% w/v, 11% w/v, 4% w/v

OLIMEL 7.6% E

Amino acids **WITH** electrolytes, dextrose, lipids
Injectable Emulsion
7.6% w/v & 0.8% w/v, 7.3% w/v, 3.5% w/v

PeriOLIMEL 2.5% E

Amino acids **WITH** electrolytes, dextrose, lipids
Injectable Emulsion
2.5% w/v & 0.4% w/v, 7.5% w/v, 3% w/v

Intravenous Nutritive Supplements

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Canada

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RECENT MAJOR LABEL CHANGES

| | |
|------------------------------------|---------|
| .2 CONTRADICTIONS... | 07/2023 |
| 3 WARNINGS AND PRECAUTIONS, Immune | 07/2023 |

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PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

OLIMEL E / PeriOLIMEL E (amino acids WITH electrolytes, dextrose, lipids) is indicated for parenteral nutrition for adults when oral or enteral nutrition is impossible, insufficient or contraindicated.

1.1 Pediatrics

Pediatrics (<18 years of age): There have been no studies performed in the pediatric population.

1.2 Geriatrics

Geriatrics (> 65 years of age): There are no known differences in safety and effectiveness of parenteral nutrition formulations in the adult population based upon age.

2 CONTRAINDICATIONS

The use of OLIMEL E / PeriOLIMEL E (amino acids WITH electrolytes, dextrose, lipids) is contraindicated in the following populations/situations:

- Known hypersensitivity to egg, soybean or peanut products, olive products or any of the active substances, excipients, or components of the container. For a complete listing, see the Dosage Forms, Composition and Packaging section of the product monograph.
- 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 abnormalities of amino acid metabolism
- Severe hyperlipidemia or severe disorders of lipid metabolism characterized by hypertriglyceridemia
- Hypertriglyceridemia-associated acute pancreatitis
- Severe hyperglycemia
- Hyperkalemia (see **General** in **WARNINGS AND PRECAUTIONS**).
- Hypercalcaemia (see **General** in **WARNINGS AND PRECAUTIONS**).
- Hyperphosphatemia (see **General** in **WARNINGS AND PRECAUTIONS**)
- Hyponatremia.
- Hypermagnesemia.

Ceftriaxone must not be administered simultaneously with intravenous calcium-

containing solutions, including OLIMEL E / PeriOLIMEL E, through the same infusion line (e.g. via Y-site) because of the risk of precipitation of ceftriaxone-calcium salt. If the same infusion line is used for sequential administration, the line must be thoroughly flushed with a compatible fluid between infusions.

3 DOSAGE AND ADMINISTRATION

3.1 Dosing Considerations

Dosing of OLIMEL E / PeriOLIMEL E (amino acids WITH electrolytes, dextrose, lipids) is based upon protein, energy, and electrolyte requirements of the individual patient.

Some patients with renal and hepatic disease may benefit from reduced protein intakes.

Some patients with diabetes mellitus or glucose intolerance may benefit from reduced carbohydrate intake.

Patients with parenteral nutrition induced liver disease may benefit from reduction in lipid intake.

Patients with renal disease have decreased capacity to excrete potassium, magnesium, and phosphorus. Levels of these electrolytes should be carefully monitored in these patients.

3.2 Recommended Dose and Dosage Adjustment

Adults

Due to its high osmolarity (1120-1360 mOsmol/L), OLIMEL E must only be administered through a central vein.

Due to its low osmolarity (760 mOsmol/L), PeriOLIMEL E can be administered through a peripheral or central vein.

The dosage depends on the patient's energy expenditure, clinical status, body weight, and ability to metabolize the constituents of OLIMEL E / PeriOLIMEL E, as well as additional energy or proteins/amino acids given orally/enterally; therefore, the bag size should be chosen accordingly.

The average daily requirements in adults are:

- Protein/amino acids: 0.16 to 0.35 g nitrogen /kg body weight (1 to 2 g of amino acids/kg), depending on the patient's nutritional status and degree of catabolic stress. Special populations may require up to 0.4 g nitrogen/kg body weight (2.5 g of amino acids/kg).
- Energy: 20 to 40 kcal/kg,
- Fluid: 20 to 40* mL fluid /kg, or 1 to 1.5 mL per expended kcal.

*This is dependent on not over feeding the patient calories or protein.

The maximum daily dose should not be exceeded. Due to the static composition of the multi-chamber bag, the ability to simultaneously meet all nutrient needs of the patient may not be possible. Clinical situations may exist where patients require amounts of nutrients varying from the composition of the static bag. In this situation the impact of any volume (dose) adjustments must take into consideration the resultant effect this will have on the dosing of all other nutrient components of OLIMEL E / PeriOLIMEL E products. For example, patients may require greater than 0.2 mmol/kg/day of phosphate. In those situations, healthcare professionals may consider adjusting the volume (dose) of OLIMEL E / PeriOLIMEL E in order to meet these increased requirements.

The reconstituted emulsion provides the following for each of the formulations and bag sizes:

PeriOLIMEL 2.5%E

| | 1000 mL | 1500 mL | 2000 mL | 2500 mL |
|--|------------|------------|------------|------------|
| Lipids | 30 g | 45 g | 60 g | 75 g |
| Amino acids | 25.3 g | 38.0 g | 50.6 g | 63.3 g |
| Nitrogen | 4.0 g | 6.0 g | 8.0 g | 10.0 g |
| Dextrose Anhydrous | 75.0 g | 112.5 g | 150.0 g | 187.5 g |
| Energy: | | | | |
| Total calories approx. | 700 kcal | 1050 kcal | 1400 kcal | 1750 kcal |
| Non-amino acid calories approx. | 600 kcal | 900 kcal | 1200 kcal | 1500 kcal |
| Glucose calories | 300 kcal | 450 kcal | 600 kcal | 750 kcal |
| Lipid calories approx. ⁽¹⁾ | 300 kcal | 450 kcal | 600 kcal | 750 kcal |
| Non-amino acid calories / nitrogen ratio | 150 kcal/g | 150 kcal/g | 150 kcal/g | 150 kcal/g |
| Glucose / lipid calories ratio | 50/50 | 50/50 | 50/50 | 50/50 |
| Lipid / total calories | 43% | 43% | 43% | 43% |
| Electrolytes: | | | | |
| Sodium | 21 mmol | 31.5 mmol | 42 mmol | 52.5 mmol |
| Potassium | 16.0 mmol | 24.0 mmol | 32.0 mmol | 40.0 mmol |
| Magnesium | 2.2 mmol | 3.3 mmol | 4.4 mmol | 5.5 mmol |
| Calcium | 2.0 mmol | 3.0 mmol | 4.0 mmol | 5.0 mmol |
| Phosphate ⁽²⁾ | 8.5 mmol | 12.7 mmol | 17.0 mmol | 21.2 mmol |
| Acetate | 27 mmol | 41 mmol | 55 mmol | 69 mmol |
| Chloride | 24 mmol | 37 mmol | 49 mmol | 61 mmol |
| pH approx. | 6.4 | 6.4 | 6.4 | 6.4 |
| Osmolarity approx. | 760 mosm/L | 760 mosm/L | 760 mosm/L | 760 mosm/L |

¹ Includes calories from purified egg phosphatides

² Includes phosphate provided by the lipid emulsion

OLIMEL 3.3%E

| | 1500 mL | 2000 mL | 2500 mL |
|--|----------------|----------------|----------------|
| Lipids | 60 g | 80 g | 100 g |
| Amino acids | 49.4g | 65.8 g | 82.3 g |
| Nitrogen | 7.8 g | 10.4 g | 13.0 g |
| Dextrose Anhydrous | 172.5 g | 230.0 g | 287.5 g |
| Energy: | | | |
| Total calories approx. | 1490 kcal | 1980 kcal | 2480 kcal |
| Non-amino acid calories approx. | 1290 kcal | 1720 kcal | 2150 kcal |
| Glucose calories | 690 kcal | 920 kcal | 1150 kcal |
| Lipid calories approx. ⁽¹⁾ | 600 kcal | 800 kcal | 1000 kcal |
| Non-amino acid calories/nitrogen ratio | 165 kcal/g | 165 kcal/g | 165 kcal/g |
| Glucose / lipid calories ratio | 53/47 | 53/47 | 53/47 |
| Lipid /total calories | 47% | 47% | 47% |
| Electrolytes: | | | |
| Sodium | 52.5 mmol | 70.0 mmol | 87.5 mmol |
| Potassium | 45.0 mmol | 60.0 mmol | 75.0 mmol |
| Magnesium | 6.0 mmol | 8.0 mmol | 10.0 mmol |
| Calcium | 5.3 mmol | 7.0 mmol | 8.8 mmol |
| Phosphate ⁽²⁾ | 22.5 mmol | 30.0 mmol | 37.5 mmol |
| Acetate | 55 mmol | 73 mmol | 91 mmol |
| Chloride | 68 mmol | 90 mmol | 113 mmol |
| pH approx. | 6.4 | 6.4 | 6.4 |
| Osmolarity approx. | 1120 mosm/L | 1120 mosm/L | 1120 mosm/L |

¹ Includes calories from purified egg phosphatides

² Includes phosphate provided by the lipid emulsion

OLIMEL 4.4%E

| | 1000 mL | 1500 mL | 2000 mL |
|---|----------------|----------------|----------------|
| Lipids | 40 g | 60 g | 80 g |
| Amino acids | 44.3 g | 66.4 g | 88.6 g |
| Nitrogen | 7.0 g | 10.5 g | 14.0 g |
| Dextrose Anhydrous | 140.0 g | 210.0 g | 280.0 g |
| Energy: | | | |
| Total calories approx. | 1140 kcal | 1710 kcal | 2270 kcal |
| Non-amino acid calories approx. | 960 kcal | 1440 kcal | 1920 kcal |
| Glucose calories | 560 kcal | 840 kcal | 1120 kcal |
| Lipid calories approx. ⁽¹⁾ | 400 kcal | 600 kcal | 800 kcal |
| Non-amino acid calories/ nitrogen ratio | 137 kcal/g | 137 kcal/g | 137 kcal/g |
| Glucose / lipid calories ratio | 58/42 | 58/42 | 58/42 |
| Lipid / total calories | 35% | 35% | 35% |
| Electrolytes: | | | |
| Sodium | 35.0 mmol | 52.5 mmol | 70.0 mmol |
| Potassium | 30.0 mmol | 45.0 mmol | 60.0 mmol |
| Magnesium | 4.0 mmol | 6.0 mmol | 8.0 mmol |
| Calcium | 3.5 mmol | 5.3 mmol | 7.0 mmol |
| Phosphate | 15.0 mmol | 22.5 mmol | 30.0 mmol |
| Acetate | 45 mmol | 67 mmol | 89 mmol |
| Chloride | 45 mmol | 68 mmol | 90 mmol |
| pH approx. | 6.4 | 6.4 | 6.4 |
| Osmolarity approx. | 1360 mosm/L | 1360 mosm/L | 1360 mosm/L |

¹ Includes calories from purified egg phosphatides

OLIMEL 5.7%E

| | 1000 mL | 1500 mL | 2000 mL |
|--|----------------|----------------|----------------|
| Lipids | 40 g | 60 g | 80 g |
| Amino acids | 56.9 g | 85.4 g | 113.9 g |
| Nitrogen | 9.0 g | 13.5 g | 18.0 g |
| Dextrose Anhydrous | 110.0 g | 165.0 g | 220.0 g |
| Energy: | | | |
| Total calories approx. | 1070 kcal | 1600 kcal | 2140 kcal |
| Non-amino acid calories approx. | 840 kcal | 1260 kcal | 1680 kcal |
| Glucose calories | 440 kcal | 660 kcal | 880 kcal |
| Lipid calories approx. ⁽¹⁾ | 400 kcal | 600 kcal | 800 kcal |
| Non-amino acid calories / nitrogen ratio | 93 kcal/g | 93 kcal/g | 93 kcal/g |
| Glucose / lipid calories ratio | 52/48 | 52/48 | 52/48 |
| Lipid / total calories | 37% | 37% | 37% |
| Electrolytes: | | | |
| Sodium | 35.0 mmol | 52.5 mmol | 70.0 mmol |
| Potassium | 30.0 mmol | 45.0 mmol | 60.0 mmol |
| Magnesium | 4.0 mmol | 6.0 mmol | 8.0 mmol |
| Calcium | 3.5 mmol | 5.3 mmol | 7.0 mmol |
| Phosphate | 15.0 mmol | 22.5 mmol | 30.0 mmol |
| Acetate | 54 mmol | 80 mmol | 107 mmol |
| Chloride | 45 mmol | 68 mmol | 90 mmol |
| pH approx. | 6.4 | 6.4 | 6.4 |
| Osmolarity approx. | 1310 mosm/L | 1310 mosm/L | 1310 mosm/L |

¹ Includes calories from purified egg phosphatides

OLIMEL 7.6%E

| | 650 mL | 1000 mL | 1500 mL | 2000 mL |
|--|--------------|-------------|-------------|-------------|
| Lipids | 22.8 g | 35.0 g | 52.5 g | 70.0 g |
| Amino acids | 49.4 g | 75.9 g | 113.9 g | 151.9 g |
| Nitrogen | 7.8 g | 12.0 g | 18.0 g | 24.0 g |
| Dextrose Anhydrous | 47.7 g | 73.3 g | 110.0 g | 146.7 g |
| Energy: | | | | |
| Total calories approx. | 620 kcal | 950 kcal | 1420 kcal | 1900 kcal |
| Non-amino acid calories approx. | 420 kcal | 640 kcal | 960 kcal | 1280 kcal |
| Glucose calories | 190 kcal | 290 kcal | 430 kcal | 580 kcal |
| Lipid calories approx. ⁽¹⁾ | 230 kcal | 350 kcal | 530 kcal | 700 kcal |
| Non-amino acid calories / nitrogen ratio | 53 kcal/g | 53 kcal/g | 53 kcal/g | 53 kcal/g |
| Glucose / lipid calories ratio | 45/55 | 45/55 | 45/55 | 45/55 |
| Lipid / total calories | 37% | 37% | 37% | 37% |
| Electrolytes: | | | | |
| Sodium | 22.8 mmol | 35.0 mmol | 52.5 mmol | 70.0 mmol |
| Potassium | 19.5 mmol | 30.0 mmol | 45.0 mmol | 60.0 mmol |
| Magnesium | 2.6 mmol | 4.0 mmol | 6.0 mmol | 8.0 mmol |
| Calcium | 2.3 mmol | 3.5 mmol | 5.3 mmol | 7.0 mmol |
| Phosphate | 9.5 mmol | 15.0 mmol | 21.9 mmol | 29.2 mmol |
| Acetate | 46 mmol | 70 mmol | 105 mmol | 140 mmol |
| Chloride | 30 mmol | 45 mmol | 68 mmol | 90 mmol |
| pH approx. | 6.4 | 6.4 | 6.4 | 6.4 |
| Osmolarity approx. | 1270 mosm/ L | 1270 mosm/L | 1270 mosm/L | 1270 mosm/L |

¹ Includes calories from purified egg phosphatides

As a general rule, daily doses of 2 g/kg of amino acids and/or 7 g/kg of dextrose and/or 2 g/kg of lipids and/or 40 kcal/kg and/or 40 mL fluid/kg should not be exceeded, except in particular cases when specific demands exceed the usual recommendations. The first of these doses to be reached sets the maximum daily dose.

The OLIMEL E / PeriOLIMEL E formulations may be limited by fluid (40 ml/kg/day), energy (40 kcal/kg/day total calories) or amino acids intakes (2g/kg/day). In Continuous Renal Replacement (CRRT) and patients with morbid obesity, the maximal daily dose is defined by amino acids intake. The maximal daily dose delivers the following:

| | PeriOLIMEL 2.5%E | OLIMEL 3.3%E | OLIMEL 4.4% E | OLIMEL 5.7% E | OLIMEL 7.6% E | OLIMEL 7.6% E * |
|--------------------------|-----------------------------|-------------------------|--------------------------|--------------------------|--------------------------|----------------------------|
| Fluid volume (mL/kg/day) | 40 | 40 | 35 | 35 | 26 | 33 |
| Energy (kcal/kg/day) | 28 | 40 | 40 | 37 | 24.7 | 31.2 |
| Amino Acids (g/kg/day) | 1 | 1.3 | 1.5 | 2 | 2.0 | 2.5** |
| Dextrose (g/kg/day) | 3 | 4.6 | 4.9 | 3.9 | 1.9 | 2.4 |
| Lipid (g/kg/day) | 1.2 | 1.6 | 1.4 | 1.4 | 0.9 | 1.2 |
| Sodium (mmol/kg/day) | 0.8 | 1.4 | 1.2 | 1.2 | 0.9 | 1.2 |
| Potassium (mmol/kg/day) | 0.6 | 1.2 | 1.1 | 1.1 | 0.8 | 1.0 |

* In Continuous Renal Replacement (CRRT) and patients with morbid obesity

** In patients with morbid obesity, dosing is based on ideal body weight (IBW)

The maximal infusion rates for the average patient receiving OLIMEL E / PeriOLIMEL E formulations over a 24 hour administration period are as follows:

| Formulation | Maximal infusion rate | Amino acids (g/kg/hour) | Dextrose (g/kg/hour) | Lipids (g/kg/hour) |
|--------------------|----------------------------------|--|--------------------------------------|------------------------------------|
| PeriOLIMEL 2.5% E | 3.2 mL/kg/hour | 0.08 | 0.24 | 0.1 |
| OLIMEL 3.3%E | 2.1 mL/kg/hour | 0.07 | 0.24 | 0.08 |
| OLIMEL 4.4% E | 1.7 mL/kg/hour | 0.08 | 0.24 | 0.07 |
| OLIMEL 5.7% E | 1.8 mL/kg/hour | 0.1 | 0.19 | 0.07 |
| OLIMEL 7.6% E | 1.3 mL/kg/hour | 0.10 | 0.10 | 0.05 |

The flow rate should be increased gradually during the first hour. The administration flow rate must be adjusted to take into account the dose being administered, the daily volume intake and the duration of the infusion (see [OVERDOSAGE](#)).

3.3 Administration

For instructions for preparation and handling of the emulsion for infusion see [SPECIAL HANDLING INSTRUCTIONS](#).

PeriOLIMEL E can be administered through a peripheral or central vein due to its lower osmolality. OLIMEL E must be delivered through a central vein. (See [WARNINGS AND PRECAUTIONS](#))

The recommended duration of infusion for a parenteral nutrition bag is between 12 and 24 hours. Treatment with parenteral nutrition may be continued for as long as is required by the patient's clinical conditions.

Monitoring of laboratory and clinical parameters is recommended (see **WARNINGS AND PRECAUTIONS** and **Monitoring and Laboratory Tests**).

The compatibility with solutions administered simultaneously via a common end section must be ensured.

Additions:

Although there is a natural content of trace elements and vitamins in the product, the levels of such substances may not be sufficient to meet body's requirements and need to be supplemented in sufficient quantities to meet individual patient requirements and to prevent deficiencies from developing. However, no addition of any other substances or medicinal products to the bag should be made without first confirming their compatibility and/or suitability to prevent formation of precipitates, destabilization of the lipid emulsion and/or overloading of electrolytes which may result in serious adverse reactions (see **DRUG INTERACTIONS** and **SPECIAL HANDLING INSTRUCTIONS**).

For OLIMEL E / PeriOLIMEL E, calcium and phosphate ratios must be considered. Excess addition of calcium ion and/or inorganic and/or organic phosphate may result in the formation of calcium phosphate precipitates.

Iron ions should NOT be added to the bag since they may destabilize the lipid emulsion.

The electrolyte-containing OLIMEL E / PeriOLIMEL E products contain calcium ions which pose additional risk of coagulation precipitated in citrate anticoagulated/preserved blood or components.

3.4 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.

4 OVERDOSAGE

In the event of inappropriate administration (overdose and/or infusion rate higher than recommended), nausea, vomiting, chills, headache, hot flush, hyperhidrosis and electrolyte disturbances and signs of hypervolemia or acidosis 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.

Hyperglycemia, glucosuria, and heperosmolar syndrome may develop if dextrose infusion rate exceeds clearance.

In some serious cases, hemodialysis, hemofiltration or hemo-diafiltration may be necessary.

The reduced or limited ability to metabolize lipids may result in fat overload syndrome, the results of which are usually reversible after infusion of the lipid emulsion is stopped. (See **WARNINGS AND PRECAUTIONS** section).

| |
|---|
| For management of a suspected drug overdose, contact your regional poison control centre. |
|---|

5 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table – Dosage Forms, Strengths, Composition and Packaging.

| Route of Administration | Dosage Form / Strength/Composition | Non-medicinal Ingredients |
|-------------------------|---|---|
| Intravenous | <p>Emulsion for Infusion /</p> <p>OLIMEL 3.3% E Amino acids WITH electrolytes, dextrose, lipids Injectable Emulsion 3.3% w/v & 0.7% w/v, 11.5% w/v, 4% w/v</p> <p>OLIMEL 4.4% E Amino acids WITH electrolytes, dextrose, lipids Injectable Emulsion 4.4% w/v & 0.7% w/v, 14% w/v, 4% w/v</p> <p>OLIMEL 5.7% E Amino acids WITH electrolytes, dextrose, lipids Injectable Emulsion 5.7% w/v & 0.7% w/v, 11% w/v, 4% w/v</p> <p>OLIMEL 7.6% E Amino acids WITH electrolytes, dextrose, lipids Injectable Emulsion 7.6% w/v & 0.8% w/v, 7.3% w/v, 3.5% w/v</p> <p>PeriOLIMEL 2.5% E Amino acids WITH electrolytes, dextrose, lipids Injectable Emulsion 2.5% w/v & 0.4% w/v, 7.5% w/v, 3% w/v</p> | <p><u>Lipid emulsion chamber:</u></p> <p>Glycerol Nitrogen Purified egg phosphatide Sodium hydroxide for pH adjustment Sodium oleate Water for injections</p> <p><u>Amino acid with electrolytes solution chamber:</u></p> <p>Glacial acetic acid for pH adjustment Nitrogen Water for injections</p> <p><u>Dextrose (glucose) with or without calcium solution chamber:</u></p> <p>Hydrochloric acid for pH adjustment Nitrogen Water for injections</p> |

OLIMEL E / PeriOLIMEL E (amino acids WITH electrolytes, dextrose, lipids) is presented in the form of a 3-chamber bag. Each bag contains a sterile dextrose (glucose) solution with or without calcium, a sterile amino acid solution with other electrolytes and a sterile lipid emulsion as described below:

PeriOLIMEL 2.5% E

| | Content per bag | | | |
|---|------------------------|----------------|----------------|----------------|
| | 1000 mL | 1500 mL | 2000 mL | 2500 mL |
| 18.75% Dextrose solution (18.75 g/100 mL) | 400 mL | 600 mL | 800 mL | 1000 mL |
| 6.3% Amino acid solution (6.3 g/100 mL) | 400 mL | 600 mL | 800 mL | 1000 mL |
| 15% Lipid emulsion (15 g/ 100 mL) | 200 mL | 300 mL | 400 mL | 500 mL |

OLIMEL 3.3% E

| | Content per bag | | |
|---|------------------------|----------------|----------------|
| | 1500 mL | 2000 mL | 2500 mL |
| 28.75% Dextrose solution (28.75 g/100 mL) | 600 mL | 800 mL | 1000 mL |
| 8.2% Amino acid solution (8.2 g/100 mL) | 600 mL | 800 mL | 1000 mL |
| 20% Lipid emulsion (20 g/100 mL) | 300 mL | 400 mL | 500 mL |

OLIMEL 4.4% E

| | Content per bag | | |
|---|------------------------|----------------|----------------|
| | 1000 mL | 1500 mL | 2000 mL |
| 35% Dextrose solution (35 g/100 mL) | 400 mL | 600 mL | 800 mL |
| 11.1% Amino acid solution (11.1 g/100 mL) | 400 mL | 600 mL | 800 mL |
| 20% Lipid emulsion (20 g/100 mL) | 200 mL | 300 mL | 400 mL |

OLIMEL 5.7% E

| | Content per bag | | |
|---|------------------------|----------------|----------------|
| | 1000 mL | 1500 mL | 2000 mL |
| 27.5% Dextrose solution (27.5 g/100 mL) | 400 mL | 600 mL | 800 mL |
| 14.2% Amino acid solution (14.2 g/100 mL) | 400 mL | 600 mL | 800 mL |
| 20% Lipid emulsion (20 g/100 mL) | 200 mL | 300 mL | 400 mL |

OLIMEL 7.6% E

| | Content per bag | | | |
|---|------------------------|----------------|----------------|----------------|
| | 650 mL | 1000 mL | 1500 mL | 2000 mL |
| 27.5% Dextrose solution (27.5 g/100 mL) | 173 mL | 267 mL | 400 mL | 533 mL |
| 14.2% Amino acid solution (14.2 g/100 mL) | 347 mL | 533 mL | 800 mL | 1067 mL |
| 17.5% Lipid emulsion (17.5 g/100 mL) | 130 mL | 200 mL | 300 mL | 400 mL |

After mixing the contents of the three chambers, the composition per liter of the reconstituted emulsion is given in the following table for each formulation:

| Active substances | Composition per Liter of Reconstituted Emulsion | | | | |
|---|---|----------------------|--------------------|----------------------|----------------------|
| | PeriOLIMEL 2.5% E | OLIMEL 3.3% E | OLIMEL 4.4% E | OLIMEL 5.7% E | OLIMEL 7.6 % E |
| Refined olive oil + refined soybean oil ¹ | 30.00 g | 40.00 g | 40.00 g | 40.00 g | 35.00 g |
| L-Alanine | 3.66 g | 4.76 g | 6.41 g | 8.24 g | 10.99 g |
| L-Arginine | 2.48 g | 3.22 g | 4.34 g | 5.58 g | 7.44 g |
| L-Aspartic acid | 0.73 g | 0.95 g | 1.28 g | 1.65 g | 2.20 g |
| L-Glutamic acid | 1.26 g | 1.64g | 2.21 g | 2.84 g | 3.79 g |
| Glycine | 1.76 g | 2.28 g | 3.07 g | 3.95 g | 5.26 g |
| L-Histidine | 1.51 g | 1.96 g | 2.64 g | 3.40 g | 4.53 g |
| L-Isoleucine | 1.26 g | 1.64 g | 2.21 g | 2.84 g | 3.79 g |
| L-Leucine | 1.76 g | 2.28 g | 3.07 g | 3.95 g | 5.26 g |
| L-Lysine acetate (equivalent to Lysine) | 2.81 g (1.99 g) | 3.65 g (2.59 g) | 4.88 g (3.48 g) | 6.32 g (4.48 g) | 8.43 g (5.97 g) |
| L-Methionine | 1.26 g | 1.64 g | 2.21 g | 2.84 g | 3.79 g |
| L-Phenylalanine | 1.76 g | 2.28 g | 3.07 g | 3.95 g | 5.26 g |
| L-Proline | 1.51 g | 1.96g | 2.64 g | 3.40 g | 4.53 g |
| L-Serine | 1.00 g | 1.30 g | 1.75 g | 2.25 g | 3.00 g |
| L-Threonine | 1.26 g | 1.64 g | 2.21 g | 2.84 g | 3.79 g |
| L-Tryptophan | 0.42 g | 0.55 g | 0.74 g | 0.95 g | 1.26 g |
| L-Tyrosine | 0.06 g | 0.08 g | 0.11 g | 0.15 g | 0.20 g |
| L-Valine | 1.62 g | 2.10 g | 2.83 g | 3.64 g | 4.86 g |
| Sodium acetate, trihydrate | 1.16 g | 1.50 g | 1.50 g | 1.50 g | 1.50 g |
| Sodium glycerophosphate, hydrated | 1.91 g | 3.67 g | 3.67 g | 3.67 g | 3.67 g |
| Potassium chloride | 1.19 g | 2.24 g | 2.24 g | 2.24 g | 2.24 g |
| Magnesium chloride, hexahydrate | 0.45 g | 0.81 g | 0.81 g | 0.81 g | 0.81 g |
| Calcium chloride, dihydrate | 0.30 g | 0.52 g | 0.52 g | 0.52 g | 0.52 g |
| Dextrose (Glucose monohydrate) (equivalent to Glucose anhydrous) | 82.50 g (75.00 g) | 126.5 g (115.0 g) | 154.0 g (140 g) | 121.0 g (110.0 g) | 80.67 g (73.33 g) |

¹ Mixture of refined olive oil (approximately 80%) and refined soybean oil (approximately 20%) corresponding to a ratio essential fatty acids / total fatty acids of 20%.

Packaging

The three-chamber bag is a multi-layer non-Polyvinyl Chloride bag. The inner (contact) layer of the bag material is made of a blend of polyolefinic copolymers and is compatible with amino acid solutions, dextrose solutions and lipid emulsions. Other layers are made of poly-ethylene vinyl acetate, and of a copolyester.

The dextrose chamber is fitted with an injection site to be used for addition of supplements.

The amino acids compartment is fitted with an administration site for insertion of the spike of the infusion set.

To protect from air contact, the bag is packaged in an oxygen barrier overpouch, which contains an oxygen absorber.

Pack sizes:

650 mL bag: 1 carton with 10 bags

1000 mL bag: 1 carton with 6 bags

1500 mL bag: 1 carton with 4 bags

2000 mL bag: 1 carton with 4 bags

2500 mL bag: 1 carton with 2 bags

6 WARNINGS AND PRECAUTIONS

General

No substances or medicinal products other than the provided components of the products should be added to the bag without first confirming their compatibility and/or suitability to prevent formation of precipitates, destabilization of the lipid emulsion and/or overloading of electrolytes which may result in serious adverse reactions (see **DRUG INTERACTIONS** and **SPECIAL HANDLING INSTRUCTIONS**).

Due to presence of phosphate ion in OLIMEL E / PeriOLIMEL E products (amino acids WITH electrolytes, dextrose, lipids), 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. Caution must be exercised when calcium-containing agents are added in the product since this may result in formation of precipitates which can lead to serious or even fatal

reactions (See Respiratory subsection below and **SPECIAL HANDLING INSTRUCTIONS**).

The infusion must be stopped immediately if any signs or symptoms of an allergic reaction (such as fever, shivering, sweating, headache, skin rashes, or dyspnea) develop. Specific clinical monitoring is required when an intravenous nutrition infusion is started.

Infection and sepsis may occur as a result of improper use of intravenous catheters to administer parenteral formulations, poor maintenance of catheters or contaminated solutions. Immunosuppression and other conditions 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 recognise early infections. The occurrence of septic complications can be decreased with heightened emphasis on aseptic technique in catheter placement and maintenance as well as aseptic technique in nutritional formula preparation.

“Fat overload syndrome” has been reported with similar products. This may be caused by inappropriate administration (e.g. overdose and/or infusion rate higher than recommended, see **ADVERSE REACTIONS** and **OVERDOSAGE**); however, the signs and symptoms of this syndrome may also occur when the product is administered according to instructions. The reduced or limited ability to metabolize the lipids contained in OLIMEL E / PeriOLIMEL E may result in a fat overload syndrome. This syndrome is associated with a sudden deterioration in the patient's clinical condition and is characterized by hyperlipidemia, fever, jaundice, liver fatty infiltration (hepatomegaly), deteriorating liver function (hepatosplenomegaly), and hypoxia with or without respiratory insufficiency, anemia, leucopenia, thrombocytopenia, coagulation disorders and central nervous system manifestations (e.g. coma). These symptoms are usually reversible when the infusion of lipid emulsion is stopped.

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

If the final mixture is hypertonic, it may cause irritation of the vein when administered into a peripheral vein.

While PeriOLIMEL E may be administered through a peripheral or central vein, thrombophlebitis may develop if peripheral veins are used. The catheter insertion site must be monitored daily for local signs of thrombophlebitis.

OLIMEL E must only be administered through a central vein.

Do not connect bags in series in order to avoid air embolism due to possible residual gas contained in the primary bag.

Carcinogenesis and Mutagenesis

See **NON-CLINICAL TOXICOLOGY** in Part II of the Product Monograph.

Cardiovascular

Use with caution in patients with pulmonary edema or heart failure. Fluid status should be closely monitored. The level of triglyceride should be monitored to avoid hypertriglyceridemia when administering OLIMEL E / PeriOLIMEL E in patients with acute myocardial infarction.

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.

Serum triglycerides concentrations and the ability of the body to metabolize lipids must be monitored regularly. If a lipid metabolism abnormality is suspected, daily monitoring of serum triglycerides is recommended. Hypertriglyceridemia left untreated can lead to the development of pancreatitis, altered pulmonary function, and immune dysfunction.

Hypercholesterolemia may be caused by excessive amounts of phospholipids in the parenteral formula.

In the event of hyperglycemia, the infusion rate of OLIMEL E / PeriOLIMEL E must be adjusted and/or insulin administered.

Fructose

This product may contain fructose as an impurity in the dextrose material. Exercise caution when this product is used in patients with hereditary fructose intolerance. In these patients, fructose may result in hypoglycemia, metabolic acidosis, liver toxicity which manifests as vomiting, nausea, sweating, jaundice, hemorrhage, seizures or coma or even death. The severity of the reactions is dependent on the amount and duration of fructose intake.

Hyperglycemia

Rapid administration of dextrose solutions may produce substantial hyperglycemia which may result in or contribute to electrolyte losses, dehydration and hypovolemia due to osmotic diuresis and hyperosmolar syndrome. At certain clinical conditions it

also may increase the risk of hyposmotic hyponatremia by shifting of intracellular water to extracellular space. Use with caution in critically ill patients in whom hyperglycemia commonly occurs due to diabetes, impaired glucose intolerance, impaired fasting glucose, or is stress-induced. Hyperglycemia may increase the risk of cardiac complications, infection, systemic sepsis, acute renal failure and even death in certain clinical conditions, especially in acute stress conditions. In order to avoid hyperglycemia the infusion rate should not exceed the patient's ability to utilize glucose. 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.

Extravasation

Extravasation has been reported with the administration of OLIMEL E / PeriOLIMEL E.

Gastrointestinal

Patients may develop nausea or diarrhea.

Hepatic/Biliary/Pancreatic

Parenteral nutrition in general especially those containing amino acids, such as OLIMEL E / PeriOLIMEL E, 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.

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.

Elevated bilirubin and hepatic enzymes may occur in patients receiving parenteral nutrition and may result from excess administration of carbohydrate or lipid, lack of enteral nutrient stimulation, infection, or underlying disease.

Immune

Hypersensitivity to the constituents of the parenteral nutrition formulation such as egg, soybean or peanut products, amino acids, olive products, or any of the active substances, excipients, or components of the containers may occur. See **CONTRAINDICATIONS**.

Since dextrose in OLIMEL E / PeriOLIMEL E products is derived from corn, these products should not be used in patients with known allergy to corn or corn products. See **CONTRAINDICATIONS**.

Monitoring and Laboratory Tests

Monitor water and electrolyte balance, serum osmolarity, serum triglycerides, acid/base balance, blood glucose, liver and kidney function, blood count, including platelets, and coagulation parameters throughout treatment. Daily monitoring is recommended during initiation of parenteral nutrition and until the patient and laboratory measurements are stable.

Renal

Use with caution in patients with renal insufficiency. Fluid and electrolyte status should be closely monitored in these patients.

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

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. 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 distal to the in-line filter and suspected precipitate formation in the blood stream have also been reported.

In addition to inspection of the solution, the infusion set and catheter should also periodically be checked for precipitates.

If signs of pulmonary distress occur, the infusion should be stopped and medical evaluation initiated.

Parenteral nutrition containing lipid emulsions should be given cautiously to patients with acute respiratory distress syndrome.

6.1 Special Populations

6.1.1 Pregnant Women

There are no adequate data on use of OLIMEL E / PeriOLIMEL E in pregnant women. Physicians should carefully consider the potential risks and benefits for each specific patient before prescribing OLIMEL E / PeriOLIMEL E.

6.1.2 Breast-feeding

There are no adequate data on use of OLIMEL E / PeriOLIMEL E in lactating women. Physicians should carefully consider the potential risks and benefits for each specific patient

before prescribing OLIMEL E / PeriOLIMEL E.

It is unknown if the drug is excreted in human milk. Because many drugs are excreted in human milk precaution should be exercised.

6.1.3 Pediatrics

There have been no studies performed in the pediatric population.

7 ADVERSE REACTIONS

7.1 Adverse Reaction Overview

See **WARNINGS AND PRECAUTIONS**.

7.2 Clinical Trial Adverse Reactions

Because clinical trials are conducted under very specific conditions the adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse drug reaction information from clinical trials is useful for identifying drug-related adverse events and for approximating rates.

The safety and clinical efficacy of OLIMEL (amino acids WITH electrolytes, dextrose, lipids) was assessed in a double-blind randomized controlled study over five days. Fifty-six (56) patients requiring parenteral nutrition were enrolled, of whom twenty-eight (28) were treated with OliClinomel (a triple-chamber parenteral nutrition product similar to OLIMEL, that contains the same olive oil/soybean oil lipid, a similar amino acid profile, and dextrose) and twenty-eight (28) were treated with OLIMEL. The goal of the study was to provide information on the safety and nutritional efficacy of OLIMEL in a clinical setting.

A total of fifty-three (53) adverse events occurred during treatment; twenty-nine (29) adverse events were observed in fourteen (14) patients in the OLIMEL group versus twenty-four (24) adverse events observed in eleven (11) patients in the OliClinomel (control) group. Of the twenty-nine (29) adverse events observed in the OLIMEL group, seven (7) adverse events were designated as related to treatment. Of the twenty-four (24) adverse events observed in the OliClinomel (control) group, seven (7) patients presented with adverse events that were reported as related to treatment.

Summary of Treatment-Related Adverse Drug Reactions in the OLIMEL Study

| System Organ Class | Adverse Event | Reported Incidence by Treatment Group | | | |
|--|--------------------------------------|---------------------------------------|------|--|------|
| | | OLIMEL (n=28) up to 40 mL/kg/day | | OLICLINOMEL (n=28) up to 40 mL/kg/day | |
| | | N* | % | N* | % |
| Cardiac disorders | Tachycardia | 1 | 3.57 | 0 | 0.00 |
| Gastrointestinal disorders | Abdominal pain | 1 | 3.57 | 0 | 0.00 |
| | Diarrhea | 1 | 3.57 | 1 | 3.57 |
| | Nausea | 1 | 3.57 | 0 | 0.00 |
| Immune system disorders | Hypersensitivity | 0 | 0.00 | 1 | 3.57 |
| Investigations | Blood alkaline phosphatase increased | 0 | 0.00 | 1 | 3.57 |
| | Gamma-glutamyltransferase increased | 0 | 0.00 | 1 | 3.57 |
| Metabolism and nutrition disorders | Decreased appetite | 1 | 3.57 | 0 | 0.00 |
| | Hypertriglyceridemia | 1 | 3.57 | 0 | 0.00 |
| Renal and urinary disorders | Azotemia | 0 | 0.00 | 1 | 3.57 |
| Respiratory, thoracic and mediastinal disorders | Respiratory failure | 0 | 0.00 | 1 | 3.57 |
| Vascular disorders | Hemodynamic instability | 0 | 0.00 | 1 | 3.57 |
| | Hypertension | 1 | 3.57 | 0 | 0.00 |

*Number of patients reporting the related event

7.3 Post-Market Adverse Reactions

In addition, the following adverse reactions have been reported in the postmarketing experience, listed by MedDRA System Organ Class (SOC), then by Preferred Term (PT) in order of severity.

GASTROINTESTINAL DISORDERS: Vomiting

SKIN AND SUBCUTANEOUS SKIN DISORDERS: Rash

GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS: Injection site extravasation, Pyrexia, Chills

Class Reactions

The following adverse reactions have been reported with similar products:

Pruritus, Fat overload syndrome, Cholestasis, Elevated liver enzymes and Azotemia

Pulmonary vascular precipitates (pulmonary vascular emboli and pulmonary distress) (see **WARNINGS AND PRECAUTIONS**)

8 DRUG INTERACTIONS

8.1 Overview

No interaction studies have been performed with OLIMEL E / PeriOLIMEL E (amino acids WITH electrolytes, dextrose, lipids).

OLIMEL E / PeriOLIMEL E must not be administered simultaneously with blood through the same infusion tubing because of the risk of pseudoagglutination.

8.2 Drug-Drug Interactions

The drugs listed in this table are based on either drug interaction case reports or studies, or potential interactions due to the expected magnitude and seriousness of the interaction (i.e., those identified as contraindicated).

Table - Established or Potential Drug-Drug Interactions

| <Proper/Common name> | Source of Evidence | Effect | Clinical comment |
|---|---------------------------|--------------------------------|---|
| COUMADIN (or coumarin derivatives including warfarin) | T | Decreased anticoagulant effect | Soybean oil has a natural content of vitamin K that may counteract the anticoagulant activity of coumarin derivatives, including warfarin. Levels of vitamin K vary in the formulation. Caution is warranted and therapeutic monitoring of coagulation status is recommended. |

| | | | |
|-------------|---|-------------------|--|
| Ceftriaxone | T | Precipitate forms | Ceftriaxone must not be administered with intravenous calcium-containing solutions, including OLIMEL E / PeriOLIMEL E, through the same infusion line (e.g. via Y-site) because of the risk of precipitation of ceftriaxone-calcium salt. If the same line is used for sequential administration, the line must be thoroughly flushed with a compatible fluid between infusions. |
|-------------|---|-------------------|--|

Legend: C = Case Study; CT = Clinical Trial; T = Theoretical

Due to the potassium content of OLIMEL E / PeriOLIMEL E special care should be taken in patients simultaneously treated with potassium sparing diuretics (e.g., amiloride, spironolactone, triamterene) with ACE inhibitors, angiotensin II receptor antagonists, or the immunosuppressants tacrolimus and cyclosporine in view of the risk of hyperkalemia. This only applies to products containing electrolytes.

Due to the risk of precipitation, OLIMEL E / PeriOLIMEL E should not be admixed with ampicillin or fosphenytoin.

Due to the presence of phosphate in OLIMEL E / PeriOLIMEL E and calcium ion in OLIMEL / PeriOLIMEL with electrolyte, adding calcium-containing and/or phosphate-containing products to the products may result in formation of calcium phosphate precipitates which may destabilize the emulsion status of the product (see **SPECIAL HANDLING INSTRUCTIONS**). Calcium phosphate precipitates and destabilized emulsion status of the products may result in serious health consequences.

8.3 Drug-Food Interactions

No OLIMEL E / PeriOLIMEL E - food interaction studies have been performed.

8.4 Drug-Laboratory Test Interactions

The lipids contained in this emulsion may interfere with the results of certain laboratory tests if the blood sample is taken before lipids are eliminated (these are generally eliminated after a period of 5 to 6 hours without receiving lipids). Potential assay interference associated with lipemia should be considered when interpreting the results of lipemic samples.

8.5 Drug-Lifestyle Interactions

Interactions with lifestyle have not been evaluated.

9 ACTION AND CLINICAL PHARMACOLOGY

9.1 Mechanism of Action

Amino acids administered intravenously are directly bioavailable to the body. The amino acids are transported into tissues by active transporters where they supply substrate for protein or peptide synthesis, act as regulators of various enzymes and genes, or are converted to other bioactive compounds (such as nitric oxide, glutathione, and gamma amino butyric acid). Thus, amino acids have both structural and regulatory roles within the body. Amino acids are metabolized in the liver and small quantities may be excreted unchanged through the kidneys. Nitrogen waste products from amino acid metabolism are converted to urea and excreted via the kidneys.

Dextrose, as glucose, is taken up and metabolized by all cells in the body and represents the primary energy source for the body. Glucose can be stored in the body in the form of glycogen (primarily in liver and skeletal muscle). Glucose may also be converted to fatty acids and stored as triglycerides in fat tissue. Circulating glucose levels are regulated by the interplay between insulin and glucagon, with lesser contributions from catecholamines, growth hormone, and glucocorticoids.

Fatty acids (lipid) are important energy sources for the body. The human body cannot synthesize omega-6 (linoleic acid and derivatives) or omega-3 (α -linolenic acid and derivatives) polyunsaturated fatty acids and requires these from the diet. Fatty acids are also important as substrates for membranes, precursors for bioactive molecules (such as prostaglandins), and as regulators of gene expression.

Electrolytes have many important functions in the body and are required by all cells in the body. Sodium is the primary regulator of extracellular volume and the major contributor to extracellular osmolality. Potassium is the primary determinant of the membrane electrical potential and important for protein synthesis. Calcium is essential for bone structure and function and is an important regular of cellular signalling and enzyme activity. Phosphorus is important for structure and function of many compounds, including the energy compounds, adenosine triphosphate and creatine phosphate. Magnesium is a regulator of many enzymes and a structural component of bone.

9.2 Pharmacodynamics

The content of nitrogen (amino acids) in OLIMEL E / PeriOLIMEL E (amino acids WITH electrolytes, dextrose, lipids) and energy (dextrose and triglycerides) enables maintenance of an adequate nitrogen/energy balance. Nitrogen and energy are required for normal functioning of all cells in the body, and are important for protein synthesis, growth, wound healing, immune function, muscle function, and many other cellular activities.

The amino acid solution contains 17 amino acids (including 8 essential amino acids), which are indispensable for protein synthesis. All the amino acids used in OLIMEL E / PeriOLIMEL E are

in the optical L-form, except glycine, whose molecule has no chiral center and is not optically active. The optical L-form is known to be more compatible to human biochemistry. Amino acids also represent an energy source, their oxidation resulting in excretion of nitrogen in the form of urea.

The amino acids profile is as follows:

- Essential amino acids/total amino acids: 44.8%
- Branched-chain amino acids/total amino acids: 18.3%.

Electrolytes are required for normal function of all cells in the body. These include cardiovascular, neurologic, respiratory, renal, and hepatic functions.

The lipid emulsion included in OLIMEL E / PeriOLIMEL E, is a mixture of refined olive oil and refined soybean oil (ratio 80/20), with the following approximate distribution of fatty acids:

- 15% saturated fatty acids (SFA)
- 65% monounsaturated fatty acids (MUFA)
- 20% polyunsaturated essential fatty acids (PUFA)

The phospholipid/triglyceride ratio is 0.06. The moderate essential fatty acid (EFA) content may improve utilization of infused essential fatty acids for synthesis of higher derivative fatty acids.

Olive oil contains significant amounts of alpha-tocopherol that contributes to vitamin E status.

The carbohydrate source is dextrose. Dextrose (glucose) is the primary source of energy in the body.

9.3 Pharmacokinetics

Absorption: Not applicable as this drug is given intravenously.

Distribution: The constituents of the formulation are distributed to all cells in the body.

The ingredients of OLIMEL E / PeriOLIMEL E (amino acids, electrolytes, dextrose, lipids) are distributed, metabolized and eliminated in the same manner as if they had been administered individually.

The pharmacokinetic properties of the amino acids administered intravenously are essentially the same as those of amino acids supplied by oral feeding. Amino acids from food proteins, however, first pass through the portal vein before reaching the systemic circulation.

The elimination rate of lipid emulsions depends on particle size, fatty acid composition, apolipoprotein content of the lipid globules, lipoprotein lipase activity, and hepatic lipase activity. The maximal removal capacity (K1) for the lipid emulsion found for OLIMEL E / PeriOLIMEL E in normal volunteers is 176 ± 16 mg/kg/hr. In the emulsion contained in OLIMEL E / PeriOLIMEL E, the size of the lipid particles is close to that of chylomicrons and this emulsion therefore has a similar elimination rate.

Metabolism and excretion: Amino acids, dextrose, and triglycerides are metabolized by all cells in the body. Nitrogen waste is converted to urea in the liver and excreted by the kidneys. Glucose and triglycerides are metabolized to carbon dioxide and excreted by the lungs. Electrolytes are not metabolized. They are stored in the body or excreted by the liver, intestines, kidneys, or skin.

Special Populations and Conditions

Pharmacokinetic data have not been obtained in special patient populations or conditions.

10 STORAGE, STABILITY AND DISPOSAL

Do not freeze. Store the unmixed product in the overpouch at 15°C to 30°C.

Shelf life after reconstitution:

It is recommended that the product be used immediately after the non-permanent seals between the 3 chambers have been opened.

Shelf life after addition of supplements (electrolytes, trace elements, vitamins; see **SPECIAL HANDLING INSTRUCTIONS**):

Addition of supplements must take place under controlled and validated aseptic conditions. From a microbiological point of view, any admixture should be used immediately. If not used immediately, storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2°C to 8°C.

11 SPECIAL HANDLING INSTRUCTIONS

To open

Remove the protective overpouch.

Discard the oxygen absorber.

Confirm the integrity of the bag and of the non-permanent seals. Use only if the bag is not damaged, if the non-permanent seals are intact (i.e. no mixture of the contents of the three chambers), if the amino acids solution and the dextrose solution are clear, colourless or slightly yellow, practically free of visible particles, and if the lipid emulsion is a homogeneous liquid with a milky appearance.

Mixing the solutions and the emulsion

Ensure that the product is at room temperature when breaking the non-permanent seals.

Manually roll the bag onto itself, starting at the top of the bag (hanger end). The non-permanent seals will disappear from the side near the inlets. Continue to roll until the seals are open along approximately half of their length.

Mix by inverting the bag at least 3 times.

The appearance after reconstitution is a homogeneous milk-like emulsion.

Additions

Additions must be performed under aseptic conditions and by qualified personnel.

The capacity of the bag is sufficient to enable additions of nutritional and medicinal substances such as vitamins, electrolytes and trace elements. However, other than the provided components of the product, no substance should be added to the bag without first confirming its compatibility and suitability as stated below in order to prevent formation of precipitates, destabilization of the lipid emulsion and/or overloading of electrolytes which may result in serious adverse reactions.

Any addition (including vitamins) may be made into the reconstituted mixture (after the non-permanent seals have been opened and after the contents of the three chambers have been mixed). Iron ions should NOT be added to the bag since they may destabilize the lipid emulsion of the product.

Vitamins may also be added into the dextrose chamber before the mixture is reconstituted (before opening the non-permanent seals and before mixing the solutions and the emulsion).

When making additions to PeriOLIMEL E, the final osmolarity of the mixture should be measured before administration via a peripheral vein.

OLIMEL E / PeriOLIMEL E formulations may be supplemented with electrolytes. Electrolyte supplementation should be dictated by the patient's clinical needs and should not exceed nutritional guidelines. When making additions to the formulations containing electrolytes, the amount of electrolytes already present in the bag should be taken into account. When calcium-containing and/or phosphate-containing products are added to the products, caution must be exercised to prevent formation of calcium phosphate precipitates in the reconstituted mixture AND/OR in the body after administration. The maximal total levels for sodium, magnesium, potassium and calcium listed in the tables below were demonstrated by stability data, but **should not be considered as dosage recommendations** since the safety of the resulting mixture has not been adequately studied in clinical settings. If the level of calcium and/or

phosphate in the reconstituted mixture exceeds the level shown in the following tables, the stability of the mixture may be compromised due to formation of calcium phosphate precipitates.

Additions to PeriOLIMEL 2.5% E:

| Per 1000 mL | | | |
|---------------------|-------------------------|---|------------------------------------|
| | Included level | Maximal further addition ⁽⁴⁾ | Maximal total level ⁽⁴⁾ |
| Sodium | 21 mmol | 129 mmol | 150 mmol |
| Potassium | 16 mmol | 134 mmol | 150 mmol |
| Magnesium | 2.2 mmol | 3.4 mmol | 5.6 mmol |
| Calcium | 2.0 mmol | 3.0 (1.5 ⁽²⁾) mmol | 5.0 (3.5 ⁽²⁾) mmol |
| Inorganic Phosphate | 0 mmol | 8.0 mmol | 8.0 mmol |
| Organic Phosphate | 8.5 mmol ⁽¹⁾ | - ⁽³⁾ | - ⁽³⁾ |

⁽¹⁾ Including phosphate provided by the lipid emulsion

⁽²⁾ Value in condition where inorganic phosphate is added at the maximal addition level.

⁽³⁾ Organic Phosphate as a single entity may not be currently available in Canada.

⁽⁴⁾ The values are based on stability data and should not be considered as dose recommendations.

Additions to OLIMEL 3.3% E, OLIMEL 4.4% E, OLIMEL 5.7% E:

| Per 1000 mL | | | |
|---------------------|------------------------|---|------------------------------------|
| | Included level | Maximal further addition ⁽⁴⁾ | Maximal total level ⁽⁴⁾ |
| Sodium | 35 mmol | 115 mmol | 150 mmol |
| Potassium | 30 mmol | 120 mmol | 150 mmol |
| Magnesium | 4.0 mmol | 1.6 mmol | 5.6 mmol |
| Calcium | 3.5 mmol | 1.5 (0.0 ⁽²⁾) mmol | 5.0 (3.5 ⁽²⁾)mmol |
| Inorganic Phosphate | 0 mmol | 3.0 mmol | 3.0 mmol |
| Organic Phosphate | 15 mmol ⁽¹⁾ | - ⁽³⁾ | - ⁽³⁾ |

⁽¹⁾ Including phosphate provided by the lipid emulsion

⁽²⁾ Value in condition where inorganic phosphate is added at the maximal addition level.

⁽³⁾ Organic Phosphate as a single entity may not be currently available in Canada.

⁽⁴⁾ The values are based on stability data and should not be considered as dose recommendations.

Additions to OLIMEL 7.6 % E:

| Per 1000 mL | | | |
|---------------------|------------------------|---|------------------------------------|
| | Included level | Maximal further addition ⁽⁴⁾ | Maximal total level ⁽⁴⁾ |
| Sodium | 35 mmol | 115 mmol | 150 mmol |
| Potassium | 30 mmol | 120 mmol | 150 mmol |
| Magnesium | 4 mmol | 1.6 mmol | 5.6 mmol |
| Calcium | 3.5 mmol | 1.5 (0.0 ⁽²⁾) mmol | 5.0 (3.5 ⁽²⁾) mmol |
| Inorganic Phosphate | 0 mmol | 10.0 mmol | 10.0 mmol |
| Organic Phosphate | 15 mmol ⁽¹⁾ | 10 mmol ⁽³⁾ | 25 mmol ⁽³⁾ |

⁽¹⁾ Including phosphate provided by the lipid emulsion

⁽²⁾ Value in condition where inorganic phosphate is added at the maximal addition level.

⁽³⁾ Organic Phosphate as a single entity may not be currently available in Canada.

⁽⁴⁾ The values are based on stability data and should not be considered as dose recommendations

Trace elements and vitamins:

Stability has been demonstrated up to the recommended daily dose.

Trace elements and vitamins: Stability has been demonstrated with commercially available preparations of vitamins and trace elements (containing up to 1 mg of iron). Compatibility for other additives is available upon request.

To perform an addition:

- Aseptic conditions must be observed.
- Prepare the injection site of the bag.
- Puncture the injection site and inject the additives using an injection needle or a reconstitution device.
- Mix content of the bag and the additives.

Preparation of the infusion

Only administration sets and administration lines made from DEHP-free should be used.

Aseptic conditions must be observed.

Suspend the bag.

Remove the plastic protector from the administration outlet.

Firmly insert the spike of the infusion set into the administration outlet.

Administration

For single use only. Aseptic conditions must be observed. When additions are made with inorganic phosphate, 1.2 micron filters should be used.

Only administer the product after the non-permanent seals between the three chambers have been broken and the contents of the three chambers have been mixed.

Ensure that the final emulsion for infusion does not show any evidence of phase separation.

After opening the bag, the contents should be used immediately and should not be stored for a subsequent infusion. Do not reconnect any partially used bag.

Do not connect in series in order to avoid the possibility of air embolism due to gas contained in the first bag.

Any unused product or waste material and all necessary devices must be discarded.

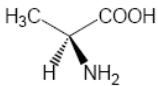
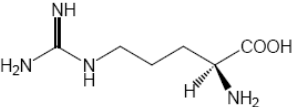
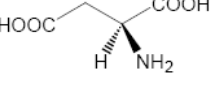
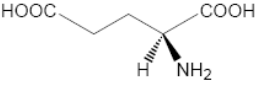
PART II: SCIENTIFIC INFORMATION

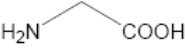
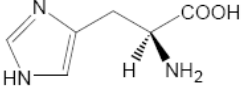
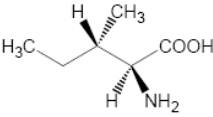
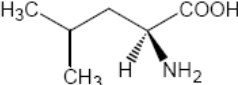
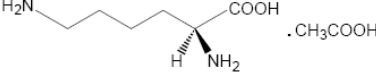
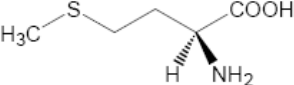
12 PHARMACEUTICAL INFORMATION

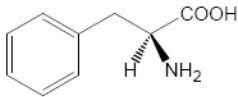
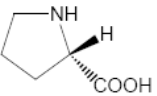
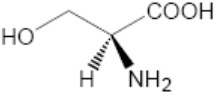
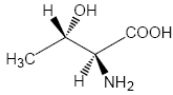
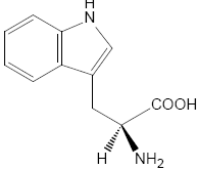
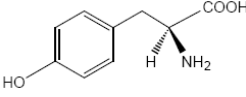
Drug Substance

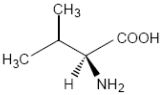
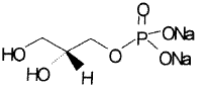
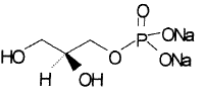
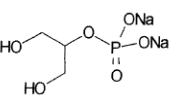

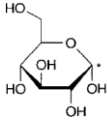
OLIMEL E / PeriOLIMEL E (amino acids WITH electrolytes, dextrose, lipids) contains the following drug substances in the three chambers.

- Dextrose solution with or without calcium (larger outer chamber)
- Amino acid solution with electrolytes (sodium, potassium, magnesium, phosphate) (centre chamber)
- Lipid emulsion (a mix of refined olive oil and refined soybean oil) (smaller outer chamber)

| Proper Name Chemical Name | Molecular Formula and Molecular Mass | Structural Formula | Physicochemical Properties |
|--|--|---|--|
| L-Alanine (S)-2-aminopropionic acid | C ₃ H ₇ NO 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 ₆ H ₁₄ N ₄ O ₂ 174.20 |  | White or almost white crystalline powder or colourless crystals, freely soluble in water, very slightly soluble in alcohol. |
| L-Aspartic Acid (S)-aminosuccinic acid | C ₄ H ₇ NO ₄ 133.10 |  | White or almost white crystalline powder or colourless crystals, slightly soluble in water, practically insoluble in alcohol. It dissolves in dilute mineral acids and in dilute solutions of alkali hydroxides. |
| L-Glutamic Acid (S)-2-aminoglutaric acid | C ₅ H ₉ NO ₄ 147.13 |  | White crystalline powder or colourless crystals, freely soluble in boiling water, slightly soluble in cold water, practically insoluble in acetic acid, in acetone and in alcohol. |

| Proper Name Chemical Name | Molecular Formula and Molecular Mass | Structural Formula | Physicochemical Properties |
|---|---|--|--|
| 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 Acetate (2S)-2,6-diaminohexanoic acid monoacetate | $C_6H_{14}N_2O_2 \cdot C_2H_4O_2$ 206.24 |  | White or almost white crystalline powder or colourless crystals, freely soluble in water, very slightly soluble in ethanol (96%). |
| 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. |

| Proper Name Chemical Name | Molecular Formula and Molecular Mass | Structural Formula | Physicochemical Properties |
|---|--|--|---|
| L-Valine (2S)-2-amino-3-methylbutanoic acid | C ₅ H ₁₁ NO ₂ 117.15 |  | White or almost white crystalline powder or colourless crystals, soluble in water, very slightly soluble in ethanol. |
| Sodium glycerophosphate, hydrated Mixture of Sodium (2RS)-2,3-dihydroxypropyl phosphate and Sodium 2-hydroxy-1-(hydroxymethyl)-ethyl phosphate | C ₃ H ₇ Na ₂ O ₆ P·xH ₂ O degree of hydration: x=4 to 6 216.0 (anhydrous) | <p><i>R</i>-α-isomer</p>  <p><i>S</i>-α-isomer</p>  <p>β-isomer</p>  | White crystalline powder or crystals, freely soluble in water, practically insoluble in acetone and in alcohol. |
| Sodium acetate trihydrate | C ₂ H ₃ NaO ₂ ·3H ₂ O 136.08 |  | Colourless crystals, very soluble in water, soluble in alcohol. |
| Potassium chloride | KCl 74.55 | 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 ·6H ₂ O 203.30 | not provided | Colourless crystals, hygroscopic, very soluble in water, freely soluble in alcohol. |
| Calcium chloride dihydrate | CaCl ₂ ·2H ₂ O 147.01 | not provided | White crystalline powder, hygroscopic, freely soluble in water, soluble in alcohol. |
| Dextrose D-glucose monohydrate | C ₆ H ₁₂ O ₆ ·H ₂ O 198.2 |  and epimer at C* , H ₂ O | White crystalline powder with a sweet taste, freely soluble in water, sparingly soluble in alcohol. |

| Proper Name Chemical Name | Molecular Formula and Molecular Mass | Structural Formula | Physicochemical Properties |
|------------------------------|--|--|--|
| Olive oil, refined | Complex mixture of triglycerides; predominant fatty acids in olive oil are oleic, palmitic and linoleic. Approximately 870 g/mol depending on the fatty acid composition. | $\begin{array}{c} \text{CH}_2\text{-OCO-R}_1 \\ \\ \text{CH-OCO-R}_2 \\ \\ \text{CH}_2\text{-OCO-R}_3 \end{array}$ where R ₁ , R ₂ and R ₃ represent the fatty acids linked to the glycerol moiety of the triglyceride. | Clear, colourless or greenish-yellow, transparent liquid, practically insoluble in ethanol (96%), miscible with light petroleum (50°C to 70°C). When cooled, it begins to become cloudy at 10°C and becomes a butter-like mass at about 0°C. It has a relative density of about 0.913. |
| Soybean oil, refined | Complex mixture of triglycerides; predominant fatty acids in soybean oil are linoleic, oleic, palmitic and linolenic. Approximately 870 g/mol depending on the fatty acid composition. | $\begin{array}{c} \text{CH}_2\text{-OCO-R}_1 \\ \\ \text{CH-OCO-R}_2 \\ \\ \text{CH}_2\text{-OCO-R}_3 \end{array}$ where R ₁ , R ₂ and R ₃ represent the fatty acids linked to the glycerol moiety of the triglyceride. | Clear, pale yellow, liquid, miscible with light petroleum (50°C to 70°C), practically insoluble in alcohol. It has a relative density of about 0.922 and a refractive index of about 1.475. |

13 CLINICAL TRIALS

13.1 Trial Design and Study Demographics

Study ICS1063B/P01/03/Mu.F was a prospective randomized double-blind multicenter study performed to evaluate safety and nutritional efficacy of OLIMEL 5.7% (amino acids, dextrose, lipids) compared to OLICLINOMEL N8-800 (a triple chambered bag established in Europe that contains the same olive oil/soybean oil lipid, a similar amino acid profile, and dextrose). The study was conducted in a variety of patients (primarily post-surgery and trauma) who required balanced parenteral nutrition representing at least 50% of the daily nonprotein energy requirements for 5 days. The primary nutritional efficacy endpoint was transthyretin (pre-albumin) levels. Safety was evaluated using adverse events, vital signs, and biochemical markers for renal (urea, creatinine), hepatic (ASAT, ALAT, alkaline phosphatase, GGT, bilirubin), hematologic (RBC count, hemoglobin, hematocrit, platelets, WBCs, lymphocytes, neutrophils, monocytes, eosinophils, basophils) organ functions as well as glucose and lipid parameters (triglycerides, cholesterol).

| Summary of patient demographics for clinical trials in specific indication | | | | | |
|--|--|---|--|--|---|
| Study # | Trial design | Dosage, route of administration and duration | Study subjects (n=number) | Mean age (Range) | Gender |
| ICS106 3B/P01/03/Mu.F | Prospective randomized double-blind multicenter controlled trial | OLIMEL 5.7%: 29 kcal/kg/day; protein 1.5 g/kg/day; 5 days OLICLINOMEL: 29 kcal/kg/day; protein 1.5 g/kg/day ; 5 days via central vein | ITT population OLIMEL 5.7%: n=24 OLICLINOMEL: n=26 | OLIMEL 5.7%: 56±15 years OLICLINOMEL: 52±21 years | OLIMEL 5.7%: 17 male, 7 female OLICLINOMEL: 16 male, 10 female |

13.2 Study Results

Results of study ICS1063B/P01/03/Mu.F in specific indication

| Primary Endpoints | Associated value and statistical significance for Drug at specific dosages | Associated value and statistical significance for Placebo or active control |
|----------------------|---|---|
| Transthyretin levels | No differences were found between the two nutritional groups for transthyretin levels. Day 1 to Day 5: 144±75 mg/L to 206±142 mg/L | Day 1 to day 5: 146±83 mg/L to 181±82 mg/L |

Adverse events were similar between groups (see [Clinical Trial Adverse Reactions](#)). There were no differences between groups for glucose, lipids, renal function, hepatic function, or hematologic function.

14 NON-CLINICAL TOXICOLOGY

Studies on the carcinogenic potential, reproductive and developmental toxicity, and genotoxic potential have not been performed on the finished product for OLIMEL E / PeriOLIMEL E (amino acids WITH electrolytes, dextrose, lipids).

Amino Acid Compartment

The amino acid solution with electrolytes contains sodium glycerophosphate as a source of nutritional phosphorus. Single-dose and 28-day repeated dose toxicity studies have been performed in rats and dogs with sodium glycerophosphate.

Single-dose Toxicity

Rats received a single intravenous bolus infusion of sodium glycerophosphate at doses of 625, 1,250 or 2,500 mg/kg. At the 2500 mg/kg dose, 10% mortality and clinical signs of toxicity were observed. Therefore, 1250 mg/kg was identified as the maximum tolerated dose following intravenous infusion in rats.

Dogs were given a single intravenous bolus infusion at doses of 625, 1250 or 1875 mg/kg. At the 1875 mg/kg dose, vomiting, jaw discomfort, half-closed eyes, loss of balance and sneezing were observed during, or just after dosing. Vomiting was noted during infusion in the 1250 mg/kg group. The no observed effect level was considered to be 625 mg/kg/day.

Repeat-Dose Toxicity

Rats were given 312.5, 625, or 1250 mg/kg of sodium glycerophosphate intravenously daily for 28 consecutive days. No test article-related changes were observed.

Dogs received sodium glycerophosphate by daily intravenous infusion at the dose-levels of 312.5, 625 or 1250 mg/kg/day for 28 consecutive days. At 1250 mg/kg/day, vomiting, rubbing of the head on the floor, shaking head, scratching of ear(s), half-closed eyes, loss of balance, sitting position and lateral recumbency were observed primarily during the first two days of the treatment period. A slight prolongation of the QT and QTc interval durations was noted in females given 1250 mg/kg/day throughout the treatment period. An increased QT interval at the 1250 mg/kg dose could be attributed to a transient, localized hypocalcemia associated with the rapid administration rate (compared to the therapeutic rate of sodium glycerophosphate delivery in humans). Sodium glycerophosphate was clinically well tolerated and did not cause any laboratory or histopathological changes at the indicated doses.

Lipid Compartment

Single-dose Toxicity

Single-dose toxicity was investigated in the mouse and rat to compare the LD₅₀ of the lipid emulsion in OLIMEL E / PeriOLIMEL E with that of 20% soybean based emulsions.

LD₅₀ values were comparable at around 100-112 mL/kg (corresponding to approximately 20 g lipid/kg) in both species with rapid infusion.

Repeat-Dose Toxicity

The lipid emulsion in OLIMEL E / PeriOLIMEL E was administered to rats and dogs by intravenous infusion in studies lasting up to 91 days. The key studies conducted and the notable findings are presented in the table below.

Repeated Dose Toxicity Studies

| Type of Study | Species and Strain | Method of Administration | Duration of Dosing | Doses (mL/kg/day) | Key Findings |
|----------------------------------|---------------------------------------|--------------------------|--------------------|--|---|
| 30 Day toxicity study in the rat | Rat Sprague Dawley CD (Charles River) | IV infusion | 30 days | 90 at a rate of 1.2 mL/kg/min | Hematuria Decreased food consumption Regenerative anemia Mild thrombocytopenia Increased hepatic enzymes Increased serum cholesterol and phospholipids Hepatocellular vacuolation and necrosis Hepatic and splenic macrophage pigmentation Splenic macrophage vacuolation Interstitial and tubular nephritis |
| 30 Day toxicity study in the rat | Rat Sprague Dawley CD (Charles River) | IV infusion | 30 days | 75 at a rate of 1.5 mL/kg/min | Hematuria Decreased food consumption Regenerative anemia Mild thrombocytopenia Increased hepatic enzymes Increased serum phospholipids Hepatic vacuolation and inflammation Hepatic and splenic macrophage pigmentation Splenic macrophage vacuolation Interstitial and tubular nephritis |
| 90 Day toxicity study in the rat | Rat Sprague Dawley CD (Charles River) | IV infusion | 90 days | 15, 30 and 60 at a rate of 2 mL/kg/min | Hematuria Decreased food consumption Mild anemia at 60 mL/kg Dose-dependent hepatic vacuolation and inflammation Hepatic and splenic macrophage pigmentation Splenic macrophage vacuolation |

| Type of Study | Species and Strain | Method of Administration | Duration of Dosing | Doses (mL/kg/day) | Key Findings |
|----------------------------------|--------------------|--------------------------|--------------------|-------------------------------|---|
| 30 Day toxicity study in the dog | Dog Beagle | IV infusion | 30 days | 45 at a rate of 0.2 mL/kg/min | Decreased food consumption Increased hepatic enzymes Increased serum cholesterol and phospholipids Hepatocellular vacuolation Hepatic and splenic macrophage pigmentation Splenic macrophage vacuolation |
| 30 Day toxicity study in the dog | Dog Beagle | IV infusion | 30 days | 60 at a rate of 0.2 mL/kg/min | Decreased food consumption Regenerative anemia Mild thrombocytopenia Increased hepatic enzymes Increased serum phospholipids Hepatic vacuolation and inflammation, Hepatic and splenic macrophage pigmentation Splenic macrophage vacuolation Renal tubular vacuolation |
| 30 Day toxicity study in the dog | Dog Beagle | IV infusion | 30 days | 60 at a rate of 0.2 mL/kg/min | Decreased food consumption Regenerative anemia Mild thrombocytopenia Increased hepatic enzymes Increased serum phospholipids Hepatic vacuolation and inflammation, Hepatic and splenic macrophage pigmentation Splenic macrophage vacuolation Renal tubular vacuolation |

| Type of Study | Species and Strain | Method of Administration | Duration of Dosing | Doses (mL/kg/day) | Key Findings |
|----------------------------------|--------------------|--------------------------|--------------------|----------------------------------|---|
| 91 Day toxicity study in the dog | Dog Beagle | IV infusion | 91 days | 15, 22.5, 30 0.2 mL/kg/min | Decreased food consumption Mild anemia at 30 mL/kg Increased hepatic enzymes at ≥ 22.5 mL/kg Increased serum cholesterol and phospholipids Hepatocellular vacuolation at 30 mL/kg Hepatic and splenic macrophage pigmentation Splenic macrophage vacuolation |

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE
PATIENT MEDICATION INFORMATION

OLIMEL 3.3% E

Amino acids **WITH** electrolytes, dextrose, lipids
Injectable Emulsion
3.3% w/v & 0.7% w/v, 11.5% w/v, 4% w/v

OLIMEL 4.4% E

Amino acids **WITH** electrolytes, dextrose, lipids
Injectable Emulsion
4.4% w/v & 0.7% w/v, 14% w/v, 4% w/v

OLIMEL 5.7% E

Electrolytes
Amino acids **WITH** electrolytes, dextrose, lipids
Injectable Emulsion
5.7% w/v & 0.7% w/v, 11% w/v, 4% w/v

OLIMEL 7.6% E

Electrolytes
Amino acids **WITH** electrolytes, dextrose, lipids
Injectable Emulsion
7.6% w/v & 0.8% w/v, 7.3% w/v, 3.5% w/v

PeriOLIMEL 2.5% E

Amino acids **WITH** electrolytes, dextrose, lipids
Injectable Emulsion
2.5% w/v & 0.4% w/v, 7.5% w/v, 3% w/v

Read this carefully before you start taking OLIMEL E / PeriOLIMEL E and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about OLIMEL E / PeriOLIMEL E product.

What is OLIMEL E / PeriOLIMEL E used for?

OLIMEL E / PeriOLIMEL E is used to provide nutrition to adults. It is given to you through a tube into a vein when normal feeding by mouth is not possible or suitable.

OLIMEL E / PeriOLIMEL E will only be given to you under medical supervision.

How does OLIMEL E / PeriOLIMEL E work?

OLIMEL E / PeriOLIMEL E is given to you when you are unable to eat to get an adequate intake of energy, nitrogen and other nutrients. This helps treat or prevent malnutrition.

What are the ingredients in OLIMEL E / PeriOLIMEL E?

Medicinal ingredients:

OLIMEL E / PeriOLIMEL E product is an emulsion for infusion, supplied in a bag with three chambers.

one chamber contains a solution of 17 amino acids (L-Alanine, L-Arginine, L-Aspartic Acid, L-Glutamic Acid, Glycine, L-Histidine, L-Isoleucine, L-Leucine, L-Lysine Acetate, L-Methionine, L-Phenylalanine, L-Proline, Serine, L-Threonine, L-Tryptophan, L-Tyrosine, L-Valine) with electrolytes (sodium, potassium, magnesium, phosphate);

one chamber contains a dextrose solution with or without calcium;

one chamber contains a lipid emulsion, which is a mix of refined olive oil and refined soybean oil.

Non-medicinal ingredients:

Glacial acetic acid (for pH adjustment)

Glycerol

Hydrochloric acid (for pH adjustment)

Nitrogen

Purified egg phosphatide

Sodium hydroxide (for pH adjustment)

Sodium oleate

Water for injection

OLIMEL E / PeriOLIMEL E comes in the following dosage forms:

OLIMEL 3.3% E (3.3% w/v amino acids with 0.7% w/v electrolytes, 11.5 % dextrose, 4% w/v lipids) Injectable Emulsion

OLIMEL 4.4% E (4.4% w/v amino acids with 0.7% w/v electrolytes, 14% w/v dextrose, 4% w/v lipids) Injectable Emulsion

OLIMEL 5.7% E (5.7% w/v amino acids with 0.7% w/v electrolytes, 11% w/v dextrose, 4% w/v lipids) Injectable Emulsion

OLIMEL 7.6% E (7.6% w/v amino acids with 0.8% w/v electrolytes, 7.3% w/v dextrose, 3.5% w/v lipids) Injectable Emulsion

PeriOLIMEL 2.5% E (2.5% w/v amino acids with 0.4% w/v electrolytes, 7.5% w/v dextrose, 3% w/v lipids) Injectable Emulsion

Do not use OLIMEL E / PeriOLIMEL E if:

- You are allergic to any ingredients (such as egg, soybean or peanut proteins, olive products.) or any ingredients in OLIMEL E / PeriOLIMEL E or components of the container. (See **What the medicinal ingredients are** and **What the important nonmedicinal ingredients are**.)
- You have liver failure or coma resulting from liver failure.
- You have kidney failure and are not on dialysis
- You have an allergy to corn or corn products since this product contains dextrose from corn.
- Your body has problems processing certain amino acids that are included in OLIMEL E / PeriOLIMEL E.
- Your body has severe problems metabolizing (breaking down) fat.

- You have especially high levels of fats in your blood.
- You have acute pancreatitis (severe inflammation of pancreas) in association with hyperlipidemia (high blood fat levels).
- You have hyperglycemia (too much sugar in your blood), which is not controlled.
- You have high blood levels of one of the electrolytes included in some of the OLIMEL E / PeriOLIMEL E.
- You have a disorder resulting in high blood levels of substances such as potassium (hyperkalemia), calcium (hypercalcemia), phosphorus (hyperphosphatemia), sodium (hyponatremia) and magnesium (hypermagnesemia).
- You are being given ceftriaxone with intravenous calcium-containing solutions, including OLIMEL E / PeriOLIMEL E, through the same infusion line.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take OLIMEL E / PeriOLIMEL E. Talk about any health conditions or problems you may have, including if you:

- are allergic to any ingredients (such as egg, soybean or peanut proteins, olive products, corn.)
- suffer from metabolic acidosis (when the blood is excessively acid)
- have kidney problems
- have liver problems
- have heart problems or have had heart problems
- have lung or breathing problems
- have diabetes
- have a disorder where your body cannot break down fats properly
- have acute respiratory distress syndrome. This is a serious condition where fluid builds up in the lungs.
- are taking any other medicines on a regular basis
- are pregnant or intend to become pregnant
- are breastfeeding or intend to breastfeed
- have hereditary fructose intolerance. This is a condition where your body cannot break down fructose properly. This product may contain small amounts of fructose

Other warnings you should know about:

In all cases, your doctor will give you OLIMEL E / PeriOLIMEL E based on factors such as age, weight, condition, and any tests results that they have done. Always be sure to check with your doctor if anything about your condition changes.

Your doctor will need to monitor how you are doing while you are on this medicine. This means that you will need to have laboratory tests done on a routine basis.

Precipitates (e.g. solid particles) can appear in OLIMEL E / PeriOLIMEL E when a calcium-containing product is added to it. It has been reported that these injected precipitates can block an artery in the lungs, cause breathing difficulties and even death. Your doctor will decide with caution, whether a calcium-containing product will be mixed with OLIMEL E / PeriOLIMEL E.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with OLIMEL E / PeriOLIMEL E:

- OLIMEL E / PeriOLIMEL E must NOT be given at the same time with blood through the

- same infusion tubing
- Blood thinner medicines such as warfarin.
- Ceftriaxone, an antibiotic medicine.
- Diuretics (water pills), such as amiloride, spironolactone, triamterene
- Medicines used to treat high blood pressure or heart failure
- Medicines that affect your immune system (known as immunosuppressants) such as tacrolimus and cyclosporine
- Medicines or infusions containing calcium or phosphate.

How to take OLIMEL E / PeriOLIMEL E:

OLIMEL E / PeriOLIMEL E can be given in a hospital or managed care facility, or at home under the supervision of a doctor or other health care professional.

After appropriate training and with the agreement of your medical team, you may be able to administer OLIMEL E / PeriOLIMEL E yourself. Your doctor's instructions must be followed exactly when taking OLIMEL E / PeriOLIMEL E.

Before using the product, the bag must be prepared as shown in the pictures.

Use only if the solutions are clear, colourless or slightly yellow, practically free of visible particles and if the emulsion is homogeneous and milk-like.

Use only if the bag is not damaged and if the non-permanent seals between the chambers are intact (no mixing of the 3 chambers contents).

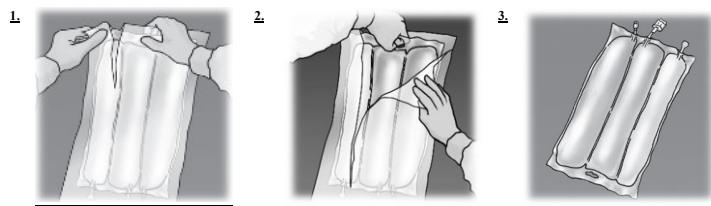
Make sure the product is at room temperature.

Aseptic conditions must be followed (cleaning of hands).

OLIMEL E must be delivered through a central vein. PeriOLIMEL E may be delivered through a central or peripheral vein.

Your healthcare professional will provide instructions on the preparation of the site and route of administration (central or peripheral vein).

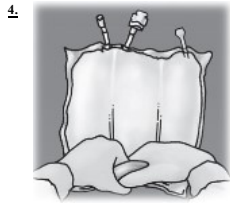
OLIMEL E / PeriOLIMEL E should only be used once. Discard unused portion, do not use a partially used bag.



1. Tear from the top to open the overpouch.

2. Peel the front of the overpouch to reveal the OLIMEL E / PeriOLIMEL E bag. Discard the overpouch and oxygen absorber.

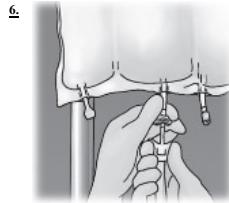
3. Place the bag flat on an horizontal and clean surface with handle in front of you.



4. Lift the hanger area to remove solution from the upper bag. Roll firmly the upper bag until peel seals are fully open (approximately half way).



5. Mix by turning the bag upside-down at least 3 times.



6. Hang the bag. Twist off the protector from the Administration outlet. Firmly plug the spike connector.

Usual adult dose:

Your doctor will select PeriOLIMEL E or the appropriate OLIMEL E for you, based on your body weight. He/she will also consider how much energy you need and how well your body can handle the amino acids, lipids, and electrolytes in the different solutions

Your doctor will also specify a flow rate corresponding to your needs and medical condition.

Always use OLIMEL E / PeriOLIMEL E exactly as your doctor has told you to. You should check with your doctor if you are not sure.

The product infusion may continue for as long as the doctor advises, depending upon your medical condition. The infusion of one triple-chamber bag usually lasts between 12 and 24 hours. The maximum daily dose should not be exceeded.

Overdose:

If your dose is too high or is infused too quickly, the following may happen:

- the amino acid content may make your blood too acidic;
- the dextrose content may increase the glucose in your blood and urine;
- the lipid content may increase the fats in your blood.

Giving too high a volume may cause nausea, vomiting, headache, hot flush, excessive sweating and shivering.

In some severe cases, your doctor may have to give you temporary renal dialysis to help your kidneys get rid of any extra nutrients.

To help prevent these events, your doctor will routinely check your condition, and test your blood and urine.

If you feel you have been given too much or have taken too much OLIMEL E / PeriOLIMEL E, contact your healthcare professional, hospital emergency department or the regional poison control centre, even if there are no symptoms.

Missed Dose:

If you miss or forget to take one or more doses of OLIMEL E / PeriOLIMEL E, contact your doctor as soon as possible. Your doctor will instruct you about how to re-start your treatment and what flow rate to use.

DO NOT take a double dose to make up for forgotten individual doses.

What are possible side effects from using OLIMEL E / PeriOLIMEL E?

These are not all the possible side effects you may feel when taking OLIMEL E / PeriOLIMEL E. If you experience any side effects not listed here, contact your healthcare professional.

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

OLIMEL E / PeriOLIMEL E can cause abnormal blood test results. Your doctor will decide when to perform blood tests and will interpret the results.

Side effects may include:

- nausea
- diarrhea
- abdominal pain
- decreased appetite
- vomiting
- rash
- fever
- chills
- itchiness

| Serious side effects and what to do about them | | | |
|---|--------------------------------------|--------------|---|
| Symptom / effect | Talk to your healthcare professional | | Stop taking drug and get immediate medical help |
| | Only if severe | In all cases | |
| UNCOMMON | | | |
| Allergic reaction: difficulty swallowing or breathing, fever, headache, shivering, skin rash or hives, shortness of breath, swelling of the face, lips, tongue or throat. | | | √ |
| Tachycardia (abnormally fast heartbeat) | | √ | |
| Azotemia (high nitrogen levels in the body): fatigue, fever, chills, nausea, swelling of feet or ankles, dark or red-coloured urine, change in how often you urinate | | | √ |
| Respiratory Failure: blue color on skin, lips, and fingernails; | | | √ |

| | | | |
|---|--|---|---|
| feel sleepy; irregular heartbeats; loss of consciousness; sudden worsening of shortness of breath | | | |
| Hypertension (high blood pressure): shortness of breath, fatigue, dizziness or fainting, chest pain or pressure, swelling in your ankles and legs, racing pulse or heart palpitations | | √ | |
| RARE | | | |
| Liver Problems: yellow colour to skin, whites of the eyes (jaundice), Abdominal pain, itching, fatigue, fever, confusion, sleepiness | | √ | |
| Decreased Platelets: bruising, bleeding, fatigue and weakness | | √ | |
| Fat Overload Syndrome (too much fat in the blood): fever, jaundice (yellowing of the skin and eyes), blood clotting, fatigue, irregular heartbeats, pale complexion, trouble breathing, coma | | | √ |
| Precipitates in the Blood Vessels Leading to or from the Lungs: difficulty breathing, shortness of breath, chest pain, coughing | | | √ |
| Injection Site Reaction: pain, redness and/or swelling at the injection site | | √ | |

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Do not freeze. Store the unmixed product in the overpouch at 15°C to 30°C.

Do not use OLIMEL E / PeriOLIMEL E after the expiry date which is printed on the container and the outer packaging (MM/YYYY). The expiry date refers to the last day of that month.

Once the seals between the three chambers have been broken and the product has been mixed, the product should be used **immediately**.

This medicine must be at room temperature to be administered.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

Keep out of reach and sight of children.

If you want more information about OLIMEL E / PeriOLIMEL E:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (<https://www.canada.ca/en/health-canada.html>); the Baxter website (Baxter.ca), or by calling 1-888-719-9955.

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

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