OLIMEL®/PERIOLIMEL®
PRODUCT INFORMATION

NAME OF THE MEDICINE

OLIMEL/PeriOLIMEL

Composition

OLIMEL/PeriOLIMEL is presented in the form of a 3-compartment bag. The individual compartments contain a glucose solution, a lipid emulsion and an amino acid solution (with/without electrolytes). In products containing electrolytes, calcium is included in the glucose solution compartment and other electrolytes are in the amino acid solution compartment. There are 5 different formulations of OLIMEL (3 with electrolytes and 2 without electrolytes) and one formulation of PeriOLIMEL. The general composition of the formulations are summarised below:

With electrolytes (E)	Without electrolytes	Nitrogen[1]	Amino acid solution[2]	Glucose solution[3]	Lipid emulsion[4]
PeriOLIMEL N4-600E	**-**	4.0g/L	6.3%	18.75%	15%
OLIMEL N5-860E	**-**	5.2g/L	8.2%	28.75%	20%
OLIMEL N7-960E	***OLIMEL N7-960***	7.0g/L	11.1%	35%	20%
OLIMEL N9-840E	***OLIMEL N9-840***	9.0g/L	14.2%	27.5%	20%

[1] prefixes N4, N5, N7, N9 refer to approx nitrogen content in g/L.
[2] contains 17 amino acids (and electrolytes if present)
[3] contains calcium if present
[4] contains refined olive oil (80%) and refined soya oil (20%)

For the detailed formulations, refer to Appendix 1.

The molecular formula and CAS (Chemical Abstract Service) registry number of the active substances are listed in Appendix 2.

DESCRIPTION

Appearance before reconstitution:

- The amino acid and glucose solutions are clear and colourless or slightly yellow
- The lipid emulsion is a homogeneous liquid with a milky appearance.

After reconstitution/mixing of the contents of the 3 compartments, OLIMEL/PeriOLIMEL is a milk-like homogeneous liquid. The composition of the 3-in-1 admixture for each of the bag presentations are provided in Appendix 1.

OLIMEL/PeriOLIMEL is a hypertonic emulsion. The osmolarity and energy contents of the formulations are as follows:

OLIMEL/ PeriOLIMEL	N4-600E	N5-860E	N7-960E	N7-960	N9-840E	N9-840
Osmolarity approx (mOsm/L)	760	1120	1360	1220	1310	1170
Energy content approx (kcal/L)	700	990	1140	1140	1070	1070

PHARMACOLOGY

Pharmacological actions

This is a 3-in-1 admixture enabling the nitrogen/energy balance to be maintained from the nitrogen source (L series amino acids) and energy in the form of glucose and essential fatty acids. 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, any other cellular activities.

The amino acids solution contains 17 amino acids (including 8 essential amino acids), which are required for protein synthesis. 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%

The formulations without electrolytes allow individual electrolyte intake to be adapted to meet specific requirements.

The lipid emulsion included in OLIMEL/PeriOLIMEL, is an association of refined olive oil and refined soya 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 improves the status of their upper derivatives while correcting EFA deficiency.

Olive oil contains significant amounts of alpha-tocopherol, when combined with a moderate PUFA intake, contributes to improve vitamin E status and reduce lipid peroxidation.

The carbohydrate source is glucose. Glucose is the primary source of energy in the body.

Pharmacokinetic properties

The ingredients of the emulsion for infusion (amino acids, glucose and lipids) are distributed, metabolised and eliminated in the same way as if they had been administered individually.

The pharmacokinetic properties of the amino acids administered intravenously are principally 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. Small lipid particles appear to delay clearance whereas they increase lipolysis by lipoprotein lipase. Most of the lipid particle sizes are in the range of chylomicrons (0.08-0.6 micrometers) with the mean diameter of less than 0.35 micrometers. However, it may contain a small fraction (up to 2.5%) of particles having a diameter of more than 0.75 micrometer.

CLINICAL TRIALS

Study ICS1063B/P01/03/Mu.F was a prospective randomised double-blind multicenter study performed in fifty six hospitalised patients (age range 18-85 years) to evaluate safety and nutritional efficacy of OLIMEL N9-840 compared to OliClinomel N8-800 (not registered in Australia but contains the same ingredients as the OliClinomel products registered in Australia). 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 (AST, ALT, 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).

Efficacy analysis on the *per protocol* (PP) and *intent-to-treat* (ITT) populations showed no difference between the OLIMEL and OliClinomel groups on the primary endpoint (transthyretin), which improved from baseline to Day 5/end of treatment.

Changes in Mean Prealbumin (Transthyretin) Levels – Study ICS1063B/P01/03/Mu.F

Treatment Group Study Population	**Mean ± SD Transthyretin Levels (g/L)**	
	Baseline	**Day 5/EOT**
OLIMEL N9-840		
Intent-to-Treat Population (n = 24)	0.144 ± 0.075	0.206 ± 0.142
Per Protocol Population (n = 24)	0.144 ± 0.075	0.206 ± 0.142
OliClinomel N8-800		
Intent-to-Treat Population (n = 26)	0.146 ± 0.083	0.181 ± 0.082
Per Protocol Population (n = 23)	0.139 ± 0.078	0.172 ± 0.080

EOT: End of treatment. SD: Standard deviation.

The safety of the two formulations was comparable. There was no difference between the treatment groups for any clinical laboratory or vital sign parameters evaluated during the study.

INDICATIONS

OLIMEL/PeriOLIMEL is indicated for parenteral nutrition for adults when oral or enteral nutrition is impossible, insufficient or contraindicated.

CONTRAINDICATIONS

Use of OLIMEL/PeriOLIMEL is contraindicated in the following situations:

- in premature neonates, infants and children less than 2 years old
- known hypersensitivity to egg or soya proteins, peanut protein, corn (maize) and corn products, components of the container, or to any of the ingredients including active substances and/or excipients
- congenital abnormalities of amino acid metabolism
- severe hyperlipidaemia or severe disorders of lipid metabolism characterised by hypertriglyceridaemia
- severe hyperglycaemia
- unstable conditions (for example, following severe post-traumatic conditions, acute phase of circulatory shock, acute myocardial infarction, severe sepsis and hyperosmolar coma)
- OLIMEL/PeriOLIMEL formulations with electrolytes must not be administered to patients with pathologically elevated plasma concentrations of sodium, potassium, magnesium, calcium and/or phosphorus.

Use with caution in patients with severe liver insufficiency, including cholestasis or elevated liver enzymes. Liver function parameters should be closely monitored.

PRECAUTIONS

The infusion must be stopped immediately if any signs or symptoms of an allergic reaction (such as fever, shivering, skin rashes or dyspnoea) develop.

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. 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.

No additions to the bag should be made without first checking the compatibility, as formation of precipitates or destabilisation of the lipid emulsion could result in vascular occlusion (see *Interactions with other medicine*).

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

"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 *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 metabolise the lipids contained in OLIMEL/PeriOLIMEL accompanied by prolonged plasma clearance may result in a fat overload syndrome. This syndrome is associated with a sudden deterioration in the patient's clinical condition and is characterised by findings such as fever, anaemia, leucopenia, thrombocytopenia, coagulation disorders, hyperlipidaemia, liver fatty infiltration (hepatomegaly), deteriorating liver function, and central nervous system manifestations (e.g. coma). The syndrome is usually reversible when the infusion of the lipid emulsion is stopped.

Ceftriaxone must not be administered simultaneously with intravenous calcium-containing solutions, including OLIMEL/PeriOLIMEL, through the same infusion line (e.g., via Y-connector) 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.

Refeeding severely undernourished patients may result in the refeeding syndrome that is characterised by the shift of potassium, phosphorus and magnesium intracellularly as the patient becomes anabolic. Thiamine deficiency and fluid retention may also develop. Careful monitoring and slowly increasing nutrient intakes while avoiding overfeeding can prevent these complications. 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 N4-600E may be administered through a peripheral vein, thrombophlebitis may develop. The catheter insertion site must be monitored daily for local signs of thrombophlebitis.

OLIMEL N5-860E, N7-960, N7-960E, N9-840 or N9-840E must only be administered through a central vein.

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

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

Do not add other medicinal products or substances to one of the three components of the bag or to the reconstituted emulsion without first confirming their compatibility and the stability of the resulting preparation (in particular, stability of the lipid emulsion).

Monitor water and electrolyte balance, serum osmolarity, serum triglycerides, acid/base balance, blood glucose, liver and kidney function, and blood count, including platelets and coagulation parameters throughout treatment.

In addition, regular clinical and laboratory tests are required particularly in cases of:

- amino acid metabolism disorders (see *CONTRAINDICATIONS*)
- hepatic insufficiency because of the risk of developing or worsening neurological disorders associated with hyperammonaemia
- renal insufficiency, particularly if hyperkalaemia is present; risk of developing or worsening metabolic acidosis and hyperazotaemia if extra-renal waste removal is not being performed
- metabolic acidosis (administration of carbohydrates is not recommended in the presence of lactic acidosis)
- diabetes mellitus: monitoring of glucose concentrations, glucosuria, ketonuria and, where applicable, adjustment of insulin dosages
- coagulation disorders
- anaemia
- hyperlipidaemia (because of the presence of lipids in the emulsion for infusion).

The blood count and coagulation factors must be monitored more carefully during long-term administration (several weeks).

<u>Cardiovascular</u>
Use with caution in patients with pulmonary oedema or heart failure. Fluid status should be closely monitored.

<u>Endocrine and metabolism</u>
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 triglyceride concentrations and the ability of the body to metabolise lipids must be checked regularly. If a lipid metabolism abnormality is suspected, monitoring of serum triglycerides is recommended as clinically necessary.

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

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.

Effect on fertility

No studies have been conducted to assess the effects of OLIMEL/PeriOLIMEL on fertility

Use in pregnancy (Category – exempt)

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

Use in lactation

There are no adequate data on the use of OLIMEL/PeriOLIMEL in lactating women. Following intravenous infusion, most of the active ingredients contained in OLIMEL/PeriOLIMEL are expected to be excreted in human milk and the safety of the breastfeeding infant has not been established. Physicians should carefully consider the potential risks and benefits for each specific patient before prescribing OLIMEL/PeriOLIMEL.

Genotoxicity/Carcinogenicity

No genotoxicity/carcinogenicity studies have been conducted with OLIMEL/PeriOLIMEL.

Effects on laboratory tests

The lipids contained in this emulsion may interfere with the results of certain laboratory tests (for example, bilirubin, lactate dehydrogenase, oxygen saturation, blood haemoglobin) if the blood sample is taken before the lipids are eliminated (these are generally eliminated after a period of 5 to 6 hours without receiving lipids).

INTERACTIONS WITH OTHER MEDICINE

No interaction studies have been performed with OLIMEL/PeriOLIMEL.

Do not add other medicinal products or substances to one of the three compartments of the bag or to the reconstituted solution/emulsion without firstly confirming their compatibility and the stability of the resulting preparation (in particular stability of the lipid emulsion or formation of precipitates).

As with any parenteral nutrition admixture, calcium and phosphate ratios must be considered. Excess addition of calcium and phosphate, especially in the form of mineral salts, may result in the formation of calcium phosphate precipitates.

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

OLIMEL/PeriOLIMEL contains calcium ions which pose additional risk of coagulation precipitated in citrate anticoagulated/preserved blood or components. This only applies to products containing electrolytes.

Soya oil has a natural content of vitamin K1 that may counteract the anticoagulant activity of coumarin derivatives, including warfarin.

Due to the potassium content of OLIMEL/PeriOLIMEL (with electrolyte formulations), special care should be taken in patients simultaneously treated with potassium sparing diuretics with ACE inhibitors, angiotensin II receptor antagonists, or the immunosuppressants tacrolimus and cyclosporin in view of the risk of hyperkalaemia.

ADVERSE EFFECTS

The safety and clinical efficacy of OLIMEL N9-840 was assessed in one double-blind randomised study with an active control over five days. Twenty-eight patients with different medical conditions (post-surgery fasting, severe malnutrition, enteral intake insufficient or forbidden) were included in the OLIMEL group and received the drug at up to 40 mL/kg/day.

The investigator judged the following seven adverse reactions as related to OLIMEL:

Clinical Trial Adverse Reactions	
System Organ Class (SOC)	**Preferred MedDRA Term**
Cardiac disorders	Tachycardia
Gastrointestinal disorders	Abdominal pain Diarrhoea Nausea
Metabolism and nutritional disorders	Decreased appetite Hypertriglyceridaemia
Vascular disorders	Hypertension

Post-marketing experience
The following adverse reactions have been reported in the Post-marketing experience, listed by MedDRA System Organ Class (SOC), then by Preferred Term in order of severity.

General disorders and administration site conditions:
- Injection site extravasation, Pyrexia, Chills.

The following adverse reactions have been reported with other similar products:
- Fat overload syndrome, Cholestasis, Elevated liver enzymes and Azotaemia.
- Pulmonary vascular precipitates (pulmonary vascular emboli and pulmonary distress)

DOSAGE AND ADMINISTRATION

For single use only. It is recommended that after opening the bag, the contents should be used immediately, and not stored for subsequent infusion.

Due to its low osmolarity (760 mOsmol/L), PeriOLIMEL N4-600E can be administered through a peripheral or central vein. Due to its high osmolarity (1120-1360 mOsmol/L), OLIMEL N5-860E, N7-960E, N7-060, N9-840E, N9-840 must only be administered through a central vein.

Although there is a natural content of trace elements and vitamins in the product, the levels are insufficient to meet body requirements and these should be added to prevent deficiencies from developing.

Adults
The dosage depends on energy expenditure, the patient's clinical status and ability to metabolise constituents of OLIMEL/PeriOLIMEL, as well as on additional energy or proteins given orally/enterally. Thus, the bag size should be then chosen with regard to the patient's body weight.

The average daily requirements for adults are:

- *Protein:* 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
- *Energy:* 20 to 40 kcal/kg
- *Fluid:* 20 to 40 mL fluid/kg or 1 to 1.5 mL per expended kcal.

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 be taken into consideration the resultant effect this will have on the dosing of all other nutrient components of OLIMEL.

The flow rate should be increased gradually during the first hour. The administration flow rate must be adjusted taking into account the dose being administered, the daily volume intake and the duration of the infusion.

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 condition.

Method of preparation
Before opening the overpouch, check the colour of the oxygen indicator. Compare it to the reference colour printed next to the OK symbol and depicted in the printed area of the indicator label. Do not use the product if the colour of the oxygen indicator does not correspond to the reference colour printed next to OK symbol.

Preparation for administration
a) To open

Remove the protective overpouch.

Discard the oxygen absorber / oxygen indicator sachet.

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 compartments), if the amino acids solution and the glucose 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.

b) 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.

After reconstitution, the mixture is a homogeneous emulsion with a milky appearance.

c) Additions

The capacity of the bag is sufficient to enable additions such as vitamins, electrolytes and trace elements. 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 compartments have been mixed). Vitamins may also be added into the glucose compartment before the mixture is reconstituted (before opening the non-permanent seals and before mixing the 3 compartments).

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

When making additions to formulations containing electrolytes, the amount of electrolytes already present in the bag should be taken into account.

Additions must be performed by qualified personnel under aseptic conditions.

PeriOLIMEL N4-600E may be supplemented with electrolytes according to the table below:

<table>
<tr><th colspan="4">Additions to PeriOLIMEL N4-600E per 1000 mL</th></tr>
<tr><th></th><th>Included level</th><th>Maximal further addition</th><th>Maximal total level</th></tr>
<tr><td>Sodium</td><td>21 mmol</td><td>129 mmol</td><td>150 mmol</td></tr>
<tr><td>Potassium</td><td>16 mmol</td><td>134 mmol</td><td>150 mmol</td></tr>
<tr><td>Magnesium</td><td>2.2 mmol</td><td>3.4 mmol</td><td>5.6 mmol</td></tr>
<tr><td>Calcium</td><td>2.0 mmol</td><td>3.0 mmol</td><td>5.0 mmol</td></tr>
<tr><td rowspan="2">Phosphate</td><td rowspan="2">8.5 mmol (*)</td><td>Inorganic Phosphate
8.0 mmol</td><td>16.5 mmol(*)</td></tr>
<tr><td>Organic Phosphate
15.0 mmol</td><td>23.5 mmol(*)</td></tr>
</table>

(*) including phosphate provided by the lipid emulsion

The OLIMEL formulations containing electrolytes – OLIMEL N5-860E, N7-960E and N9-840E may be supplemented with electrolytes according to the table below:

Additions to OLIMEL N5-860E, N7-960E and N9-840E per 1000 mL			
	Included level	**Maximal further addition**	**Maximal total level**
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 mmol	5.0 mmol
Phosphate	15 mmol (#)	Inorganic Phosphate 3.0 mmol	18 mmol(#)
		Organic Phosphate 10.0 mmol	25 mmol(#)

(#) including phosphate provided by the lipid emulsion

The OLIMEL formulations without electrolytes – OLIMEL N7-960 and N9-840 may be supplemented with electrolytes according to the table below:

Additions to OLIMEL N7-960 and N9-840 per 1000 mL			
	Included level	**Maximal further addition**	**Maximal total level**
Sodium	0 mmol	150 mmol	150 mmol
Potassium	0 mmol	150 mmol	150 mmol
Magnesium	0 mmol	5.6 mmol	5.6 mmol
Calcium	0 mmol	5.0 mmol	5.0 mmol
Phosphate	3 mmol (+)	Inorganic Phosphate 8.0 mmol	11.0 mmol(+)
		Organic Phosphate 22 mmol	25 mmol(+)

(+) Including phosphate provided by the lipid emulsion

Trace elements and vitamins: Stability has been demonstrated with commercially available preparations of vitamins and trace elements (containing up to 1 mg of iron).

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.

d) Preparation of the infusion

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.

e) Administration

For single use only.

Only administer the product after the non-permanent seals between the three compartments have been broken and the contents of the three compartments have been mixed. Ensure that the final emulsion for infusion does not show any evidence of phase separation.

After opening the bag, the content must 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 disposable devices must be discarded.

OVERDOSAGE

In the event of inappropriate administration (overdose and/or infusion rate higher than recommended), nausea, vomiting, chills and electrolyte disturbances and signs of hypervolaemia 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.

Hyperglycaemia, glucosuria, and hyperosmolar syndrome may develop if glucose infusion rate exceeds clearance.

In some serious cases, haemodialysis, haemofiltration, or haemodiafiltration may be necessary.

The reduced or limited ability to metabolise lipids may result in fat overload syndrome, the results of which are usually reversible after infusion of the lipid emulsion is stopped.

PRESENTATION AND STORAGE CONDITIONS

The three-compartment bag is a multi-layer plastic bag. The inner (contact) layer of the bag is made of a blend of polyolefinic copolymers and is compatible with amino acid solutions, glucose solutions and lipid emulsions. Other layers are made of poly-ethylene vinyl acetate (EVA) and of copolyester.

The glucose compartment is fitted with an injection site to be used for addition of supplements. The amino acid compartment is fitted with an administration site for insertion of the spike of the infusion set.

The bag is packaged in an oxygen barrier overpouch which contains an oxygen absorber/oxygen indicator sachet.

Pack sizes

Formulation	***Bag size***			
PeriOLIMEL N4-600E	1000 mL	1500 mL	2000 mL	2500 mL
OLIMEL N5-860E	–	1500 mL	2000 mL	2500 mL
OLIMEL N7-960	1000 mL	1500 mL	2000 mL	–

Formulation	***Bag size***			
OLIMEL N7-960E	1000 mL	1500 mL	2000 mL	–
OLIMEL N9-840	1000 mL	1500 mL	2000 mL	–
OLIMEL N9-840E	1000 mL	1500 mL	2000 mL	–

Note: Not all formulation and/or bag sizes may be marketed.

Storage condition
Store below 25^{o}C. Do not freeze. Store in overpouch.

After reconstitution:
It is recommended that the product is used immediately after the non-permanent seals between the 3 compartments have been opened. However, the stability of the reconstituted emulsion has been demonstrated for 7 days (between 2°C and 8°C) followed by 48 hours at temperature not exceeding 25°C.

After addition of supplements (electrolytes, trace elements and vitamins; see DOSAGE and ADMINISTRATION):
For specific admixtures, chemical and physical in-use stability has been demonstrated for 7 days (between 2°C and 8°C) followed by 48 hours at temperature not exceeding 25°C.

From a microbiological point of view, any admixture should be used immediately. If not used immediately, in-use storage times and conditions, after mixing and prior to use, are the responsibility of the user and would normally not be longer than 24 hours at 2°C to 8°C.

NAME AND ADDRESS OF THE SPONSOR

Baxter Healthcare Pty Ltd
1 Baxter Drive
Old Toongabbie
NSW 2146

POISON SCHEDULE OF THE MEDICINE

Not scheduled.

DATE OF FIRST INCLUSION IN THE AUSTRALIAN REGISTER OF THERAPEUTIC GOODS (ARTG)

9 August 2013

DATE OF MOST RECENT AMENDMENT

12 April 2016

APPENDIX 1

Composition per Litre of Reconstituted Emulsion						
Active substances	**PeriOLIMEL N4-600E**	**OLIMEL N5-860E**	**OLIMEL N7-960E**	**OLIMEL N7-960**	**OLIMEL N9-840E**	**OLIMEL N9-840**
Refined olive oil + refined soya oil*	30.00 g	40.00 g	40.00 g	40.00 g	40.00 g	40.00 g
L-Alanine	3.66 g	4.76 g	6.41 g	6.41 g	8.24 g	8.24 g
L-Arginine	2.48 g	3.22 g	4.34 g	4.34 g	5.58 g	5.58 g
L-Aspartic acid	0.73 g	0.95 g	1.28 g	1.28 g	1.65 g	1.65 g
L-Glutamic acid	1.26 g	1.64g	2.21 g	2.21 g	2.84 g	2.84 g
Glycine	1.76 g	2.28 g	3.07 g	3.07 g	3.95 g	3.95 g
L-Histidine	1.51 g	1.96 g	2.64 g	2.64 g	3.40 g	3.40 g
L-Isoleucine	1.26 g	1.64 g	2.21 g	2.21 g	2.84 g	2.84 g
L-Leucine	1.76 g	2.28 g	3.07 g	3.07 g	3.95 g	3.95 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)	4.88 g (3.48 g)	6.32 g (4.48 g)	6.32 g (4.48 g)
L-Methionine	1.26 g	1.64 g	2.21 g	2.21 g	2.84 g	2.84 g
L-Phenylalanine	1.76 g	2.28 g	3.07 g	3.07 g	3.95 g	3.95 g
L-Proline	1.51 g	1.96g	2.64 g	2.64 g	3.40 g	3.40 g
L-Serine	1.00 g	1.30 g	1.75 g	1.75 g	2.25 g	2.25 g
L-Threonine	1.26 g	1.64 g	2.21 g	2.21 g	2.84 g	2.84 g
L-Tryptophan	0.42 g	0.55 g	0.74 g	0.74 g	0.95 g	0.95 g
L-Tyrosine	0.06 g	0.08 g	0.11 g	0.11 g	0.15 g	0.15 g
L-Valine	1.62 g	2.10 g	2.83 g	2.83 g	3.64 g	3.64 g
Sodium acetate, trihydrate	1.16 g	1.50 g	1.50 g	--	1.50 g	--
Sodium glycerophosphate hydrate	1.91 g	3.67 g	3.67 g	--	3.67 g	--
Potassium chloride	1.19 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	--
Calcium chloride, dihydrate	0.30 g	0.52 g	0.52 g	--	0.52 g	--
Glucose (equivalent to Anhydrous Glucose)	82.50 g (75.00 g)	126.5 g (115.0 g)	154.0 g (140 g)	154.0 g (140 g)	121.0 g (110.0 g)	121.0 g (110.0 g)

*Mixture of refined olive oil (approximately 80%) and refined soya oil (approximately 20%), corresponding to a ratio essential fatty acids / total fatty acids of 20%. The soya oil ingredient may contain *ascorbyl palmitate* as an antioxidant in the concentration ≤0.15 mg/g of soya oil.

OLIMEL/PeriOLIMEL also contains the following excipients:

- Egg lecithin (purified egg phosphatide),
- Glycerol,
- Sodium oleate,
- Sodium hydroxide/Glacial acetic acid/Hydrochloric acid (for pH adjustment), and
- Water for injections.

After the contents of the three compartments have been mixed, the 3-in-1 admixture for each of the bag presentations provides the following:

For PeriOLIMEL N4-600E

	1000 mL	**1500 mL**	**2000 mL**	**2500 mL**
Nitrogen	4.0 g	6.0 g	8.0 g	10.0 g
Amino acids	25.3 g	38.0 g	50.6 g	63.3 g
Glucose	82.5 g	123.75 g	165.0 g	206.25 g
Lipids	30 g	45 g	60 g	75 g
Energy:				
Total calories approx.	700 kcal	1050 kcal	1400 kcal	1750 kcal
Non-protein calories approx.	600 kcal	900 kcal	1200 kcal	1500 kcal
Glucose calories	300 kcal	450 kcal	600 kcal	750 kcal
Lipid calories [(1)]	300 kcal	450 kcal	600 kcal	750 kcal
Non-protein 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	21.0 mmol	31.5 mmol	42.0 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	6.4	6.4	6.4	6.4
Osmolarity	760 mOsm/L	760 mOsm/L	760 mOsm/L	760 mOsm/L

(1) Include calories from egg lecithin (purified egg phosphatide)

(2) Includes phosphate from lipid emulsion (egg phospholipids)

For OLIMEL N5-860E

	1500 mL	**2000 mL**	**2500 mL**
Nitrogen	7.8 g	10.4 g	13.0 g
Amino acids	49.4 g	65.8 g	82.3 g
Glucose	189.75 g	253.0 g	316.25 g
Lipids	60 g	80 g	100 g
Energy:			
Total calories	1490 kcal	1980 kcal	2480 kcal
Non-protein calories	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-protein 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	6.4	6.4	6.4
Osmolarity	1120 mOsm/L	1120 mOsm/L	1120 mOsm/L

(1) Include calories from egg lecithin (purified egg phosphatide)

(2) Includes phosphate from lipid emulsion (egg phospholipids)

For OLIMEL N7-960

	1000 mL	1500 mL	2000 mL
Nitrogen	7.0 g	10.5 g	14.0 g
Amino acids	44.3 g	66.4 g	88.6 g
Glucose	154.0 g	231.0 g	308.0 g
Lipids	40 g	60 g	80 g
Energy:			
Total calories	1140 kcal	1710 kcal	2270 kcal
Non-protein calories	960 kcal	1440 kcal	1920 kcal
Glucose calories	560 kcal	840 kcal	1120 kcal
Lipid calories [(1)]	400 kcal	600 kcal	800 kcal
Non-protein 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:			
Phosphate [(2)]	3.0 mmol	4.5 mmol	6.0 mmol
Acetate	31 mmol	46 mmol	62 mmol
pH	6.4	6.4	6.4
Osmolarity	1220 mOsm/L	1220 mOsm/L	1220 mOsm/L

(1) Include calories from egg lecithin (purified egg phosphatide)

(2) Includes phosphate from lipid emulsion (egg phospholipids)

For OLIMEL N7-960E

	1000 mL	1500 mL	2000 mL
Nitrogen	7.0 g	10.5 g	14.0 g
Amino acids	44.3 g	66.4 g	88.6 g
Glucose	154.0 g	231.0 g	308.0 g
Lipids	40 g	60 g	80 g
Energy:			
Total calories	1140 kcal	1710 kcal	2270 kcal
Non-protein calories	960 kcal	1440 kcal	1920 kcal
Glucose calories	560 kcal	840 kcal	1120 kcal
Lipid calories [(1)]	400 kcal	600 kcal	800 kcal
Non-protein 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 [(2)]	15.0 mmol	22.5 mmol	30.0 mmol
Acetate	45 mmol	67 mmol	89 mmol
Chloride	45 mmol	68 mmol	90 mmol
pH	6.4	6.4	6.4
Osmolarity	1360 mOsm/L	1360 mOsm/L	1360 mOsm/L

(1) Include calories from egg lecithin (purified egg phosphatide)

(2) Includes phosphate from lipid emulsion (egg phospholipids)

For OLIMEL N9-840

	1000 mL	1500 mL	2000 mL
Nitrogen	9.0 g	13.5 g	18.0 g
Amino acids	56.9 g	85.4 g	113.9 g
Glucose	121.0 g	181.5 g	242.0 g
Lipids	40 g	60 g	80 g
Energy:			
Total calories	1070 kcal	1600 kcal	2140 kcal
Non-protein calories	840 kcal	1260 kcal	1680 kcal
Glucose calories	440 kcal	660 kcal	880 kcal
Lipid calories [(1)]	400 kcal	600 kcal	800 kcal
Non-protein 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:			
Phosphate [(2)]	3.0 mmol	4.5 mmol	6.0 mmol
Acetate	40 mmol	60 mmol	80 mmol
pH	6.4	6.4	6.4
Osmolarity	1170 mOsm/L	1170 mOsm/L	1170 mOsm/L

(1) Include calories from egg lecithin (purified egg phosphatide)

(2) Includes phosphate from lipid emulsion (egg phospholipids)

For OLIMEL N9-840E

	1000 mL	1500 mL	2000 mL
Nitrogen	9.0 g	13.5 g	18.0 g
Amino acids	56.9 g	85.4 g	113.9 g
Glucose	121.0 g	181.5 g	242.0 g
Lipids	40 g	60 g	80 g
Energy:			
Total calories	1070 kcal	1600 kcal	2140 kcal
Non-protein calories	840 kcal	1260 kcal	1680 kcal
Glucose calories	440 kcal	660 kcal	880 kcal
Lipid calories [(1)]	400 kcal	600 kcal	800 kcal
Non-protein 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 [(2)]	15.0 mmol	22.5 mmol	30.0 mmol
Acetate	54 mmol	80 mmol	107 mmol
Chloride	45 mmol	68 mmol	90 mmol
pH	6.4	6.4	6.4
Osmolarity	1310 mOsm/L	1310 mOsm/L	1310 mOsm/L

(1) Include calories from egg lecithin (purified egg phosphatide)

(2) Includes phosphate from lipid emulsion (egg phospholipids)

APPENDIX 2

Molecular formula and CAS registry number of the active substances

Active substances	***Molecular Formula***	***CAS Number***
L-Alanine	$C_3H_7NO_2$	56-41-7
L-Arginine	$C_6H_{14}N_4O_2$	74-79-3
L-Aspartic acid	$C_4H_7NO_4$	56-84-8
L-Glutamic acid	$C_5H_9NO_4$	56-86-0
Glycine	$C_2H_5NO_2$	56-40-6
L-Histidine	$C_6H_9N_3O_2$	71-00-1
L-Isoleucine	$C_6H_{13}NO_2$	73-32-5
L-Leucine	$C_6H_{13}NO_2$	61-90-5
L-Lysine acetate	$C_6H_{14}N_2O_2 \cdot C_2H_4O_2$	57282-49-2
L-Methionine	$C_5H_{11}NO_2S$	63-68-3
L-Phenylalanine	$C_9H_{11}NO_2$	63-91-2
L-Proline	$C_5H_9NO_2$	147-85-3
L-Serine	$C_3H_7NO_3$	56-45-1
L-Threonine	$C_4H_9NO_3$	72-19-5
L-Tryptophan	$C_{11}H_{12}N_2O_2$	73-22-3
L-Tyrosine	$C_9H_{11}NO_3$	60-18-4
L-Valine	$C_5H_{11}NO_2$	72-18-4
Sodium acetate, trihydrate	$C_2H_3NaO_2 \cdot 3H_2O$	6131-90-4
Sodium glycerophosphate hydrate	$C_3H_7Na_2O_6P \cdot xH_2O$ (degree of hydration: x= 4 to 6)	1334-74-3 (anhydrous)
Potassium chloride	KCl	7447-40-7
Magnesium chloride, hexahydrate	$MgCl_2 \cdot 6H_2O$	7791-18-6
Calcium chloride, dihydrate	$CaCl_2 \cdot 2H_2O$	10035-04-8
Glucose	$C_6H_{12}O_6 \cdot H_2O$	5996-10-1
Refined olive oil	Complex mixture of triglycerides; predominant fatty acids in olive oil are oleic, palmitic and linoleic.	8001-25-0
Refined soya oil	Complex mixture of triglycerides; predominant fatty acids in soya oil are linoleic, palmitic and linolenic.	8001-22-7