Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

OLICLINOMEL N 4-550E, emulsion for infusion.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

This medicinal product is presented in the form of a 3-compartment bag.
There are four presentations, which have the following different volumes:

Compartment	**1000 ml**	**1500 ml**	**2000 ml**	**2500 ml**
Lipid emulsion	200 ml	300 ml	400 ml	500 ml
Amino acid solution	400 ml	600 ml	800 ml	1000 ml
Glucose solution	400 ml	600 ml	800 ml	1000 ml

Composition of a 1000ml bag:

Active substances	**10% lipid emulsion compartment** (corresponding to 10g/100ml) **(200 ml)**	**5.5% amino acid solution compartment** (corresponding to 5.5g/100ml) **(400 ml)**	**20% glucose solution compartment** (corresponding to 20g/100ml **(400 ml)**
Refined olive oil + refined soya oil*	20.00 g		
Alanine		4.56 g	
Arginine		2.53 g	
Glycine		2.27 g	
Histidine		1.06 g	
Isoleucine		1.32 g	
Leucine		1.61 g	
Lysine (As lysine hydrochloride)		1.28 g (1.60g)	
Methionine		0.88 g	
Phenylalanine		1.23 g	
Proline		1.50 g	
Serine		1.10 g	
Threonine		0.92 g	
Tryptophan		0.40 g	
Tyrosine		0.09 g	
Valine		1.28 g	

Sodium Acetate, $3H_2O$		0.98 g	
Sodium glycerophosphate, $5H_2O$		2.14 g	
Potassium chloride		1.19 g	
Magnesium chloride, $6H_2O$		0.45 g	
Anhydrous glucose (As glucose monohydrate)			80.00g (88.00g)
Calcium chloride, $2H_2O$			0.30 g

* Mixture of refined olive oil (approximately 80%) and refined soya oil (approximately 20%)

For full list of excipients, see section 6.1

After the contents of the three compartments have been mixed, the ternary mixture for each of the bag presentations provides the following:

Per bag	**1 litre**	**1.5 litre**	**2 litres**	**2.5 litres**
Nitrogen (g)	3.6	5.4	7.3	9.1
Amino acids (g)	22	33	44	55
Glucose (g)	80	120	160	200
Lipids (g)	20	30	40	50
Total calories (kcal)	610	910	1215	1520
Non-protein calories (kcal)	520	780	1040	1300
Glucose calories (kcal)	320	480	640	800
Lipid calories (kcal)	200	300	400	500
Non-protein calorie/nitrogen ratio (kcal/g N)	144	144	144	144
Sodium (mmol)	21	32	42	53
Potassium (mmol)	16	24	32	40
Magnesium (mmol)	2.2	3.3	4.4	5.5
Calcium (mmol)	2	3	4	5
Phosphate (mmol)**	8.5	13	17	21
Acetate (mmol)	30	46	61	76
Chloride (mmol)	33	50	66	83
pH	6	6	6	6
Osmolarity (mOsm/l)	750	750	750	750

** Including phosphates provided by the lipid emulsion

3 PHARMACEUTICAL FORM

After reconstitution:
Emulsion for infusion.

Appearance prior to reconstitution:
- The lipid emulsion is an homogeneous liquid with a milky appearance,

- The amino acid and glucose solutions are clear and colourless or slightly yellow.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Parenteral nutrition for adults and children greater than 2 years of age when oral or enteral nutrition is impossible, insufficient or contraindicated.

4.2 Posology and method of administration

Posology

The dosage depends on the patient’s energy expenditure clinical status, body weight, and the ability to metabolize the constituents of OLICLINOMEL, as well as additional energy or proteins provided orally/enterally; therefore, the bag size should be chosen accordingly.

The administration may be continued for as long as is required by the patient’s clinical conditions.

In adults

Requirements:
Average nitrogen requirements are 0.16 to 0.35 g/kg/day (approximately 1 to 2 g amino acids/kg/day).
Energy requirements vary depending on the patient's nutritional state and level of catabolism. On average these are 25 to 40 kcal/kg/day.

Maximum daily dose:
The maximum daily dose is 40 ml/kg body weight (equivalent to 0.88 g amino acids, 3.2 g glucose, 0.8 g lipids, 0.84 mmol of sodium and 0.64 mmol potassium / kg), i.e. 2800 ml of the emulsion for infusion for a patient weighing 70 kg.

In children greater than two years of age

There have been no studies performed in the pediatric population.

Requirements:
Average nitrogen requirements are 0.35 to 0.45 g/kg/day (approximately 2 to 3 g amino acids/kg/day).
Energy requirements vary depending on the patient's age, nutritional state and level of catabolism. On average these range between 60 and 110 kcal/kg/day.

Posology:
The dosage is based on fluid intake and daily nitrogen requirements.
These intakes should be adjusted to take account of the child's hydration status.

Maximum daily dose:
The maximum daily dose is 100 ml/kg body weight (equivalent to 2.2 g amino acids, 8 g glucose, 2 g lipids, 2.1 mmol of sodium and 1.6 mmol potassium / kg body weight).

As a general rule do not exceed doses of 3 g/kg/day amino acids and/or 17 g/kg/day glucose and/or 3 g/kg/day lipids, except in particular cases.

Method and duration of administration

For single use only.

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

Appearance after reconstitution: Homogeneous liquid with a milky appearance.
For instructions for preparation and handling of the emulsion for infusion see section 6.6.

BY INTRAVENOUS ADMINISTRATION THROUGH A CENTRAL OR PERIPHERAL VEIN (Due to low osmolarity of OLICLINOMEL)

The recommended duration of the parenteral nutrition infusion is between 12 and 24 hours.

The administration flow rate should be adjusted to take account of the dose being administered, the characteristics of the final mixture being infused, the daily volume intake and the duration of the infusion (see section 4.4).

Normally, the flow rate should be increased gradually during the first hour.

Maximum infusion rate

As a general rule, do not exceed 3 ml/kg/hour of the emulsion for infusion, i.e. 0.06 g amino acids, 0.24 g glucose and 0.06 g lipids / kg body weight / hour.

4.3 Contraindications

The use of Oliclinomel is contraindicated in the following situations:
- In premature neonates, infants and children less than 2 years old, as the calorie-nitrogen ratio and energy supply are inappropriate.
- Hypersensitivity to egg, soybean or peanut proteins, or to any other active substance or excipients.
- Congenital abnormalities of amino acid metabolism.
- Severe hyperlipidaemia or severe disorders of lipid metabolism characterized by hypertriglyceridemia.
- Severe Hyperglycemia
- Pathologically-elevated plasma concentration of sodium, potassium, magnesium, calcium, and/or phosphorus

4.4 Special warnings and precautions for use

An excessively fast administration of total parenteral nutrition (TPN) solutions, including OLICLINOMEL, may result in severe or fatal consequences.

The infusion must be stopped immediately if any signs or symptoms of an allergic reaction (such as sweating, fever, chills, headache, skin rashes or dyspnea) develop.This medicinal product contains soybean oil and egg phosphatide. Soybean and egg proteins may cause hypersensitivity reactions. Cross-allergic reactions between soybean and peanut proteins have been observed.

Specific clinical monitoring is required when an intravenous infusion is started

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

Do not add other medicinal products or substances to any components of the bag or to the reconstituted emulsion without first confirming their compatibility and the stability of the resulting preparation (in particular, the stability of the lipid emulsion). Excess addition of calcium and phosphorus may result in the formation of calcium phosphate precipitates. Formation of precipitates or destabilization of the lipid emulsion could result in vascular occlusion (see section 6.2 and 6.6)

Vascular-access infection and sepsis are complications that may occur in patients receiving parenteral nutrition, particularly in case of poor maintenance of catheters, immunosuppressive effects of illness or drugs Careful monitoring of signs, symptoms, and laboratory tests results for fever/chills, leukocytosis, technical complications with the access device, and hyperglycemia can help recognize early infections. Patients who require parenteral nutrition are often predisposed to infectious complications due to malnutrition and/or their underlying disease state. The occurrence of septic complications can be decreased with heightened emphasis on aseptic techniques in catheter placement and maintenance, as well as aseptic techniques in the preparation of the nutritional formula.

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

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 remove lipids must be checked regularly.

Serum triglyceride concentrations must not exceed 3 mmol/l during the infusion. These concentrations should not be determined before a minimum of a 3-hour period of continuous infusion.

If a lipid metabolism abnormality is suspected, it is recommended that tests be performed daily by measuring serum triglycerides after a period of 5 to 6 hours without administering lipids. In adults, the serum must be clear in less than 6 hours after stopping the infusion containing the lipid emulsion. The next infusion should only be administered when the serum triglyceride concentrations have returned to normal values.

Fat overload syndrome has been reported with similar products. Reduced ability to remove the lipids contained in OliClinomel may result in a "fat overload syndrome" which may be caused by overdose, however, the signs and symptoms but may also occur when the product is administered according to instructions (see also section 4.8).

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

While OLICLINOMEL N4-550E may be administered through a peripheral vein, thrombophlebitis may develop. The catheter insertion site must be monitored daily for local signs of thrombophlebitis.

When making additions, the final osmolarity of the mixture must be measured before administration. The mixture obtained should be administered through a central or peripheral venous line depending on its final osmolarity. If the final mixture administered is hypertonic, it may cause irritation of the vein when administered into a peripheral 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. See instructions for making additions to this product. (See section 6.6)

Caution should be exercised in administering Oliclinomel to patients with increased osmolarity, adrenal insufficiency, heart failure or pulmonary dysfunction.

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

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

Hepatic Insufficiency
Use with caution in patients with hepatic insufficiency because of the risk of developing or worsening neurological disorders associated with hyperammonaemia. Regular clinical and laboratory tests are required particularly blood glucose, electrolytes and triglycerides.

Renal Insufficiency
Use with caution in patients with renal insufficiency, particularly if hyperkalaemia is present, because of the risk of developing or worsening metabolic acidosis and hyperazotemia if extra-renal waste removal is not being performed. Fluid, triglycerides and electrolyte status should be closely monitored in these patients.

Hematologic
Use with caution in patients with coagulation disorders and anaemia. Blood count and coagulation parameters should be closely monitored.

Endocrine and Metabolism
Use with caution in patients with:

- Metabolic acidosis. Administration of carbohydrates is not recommended in the presence of lactic acidosis. Regular clinical and laboratory tests are required.
- Diabetes mellitus. Monitor glucose concentrations, glucosuria, ketonuria and, where applicable adjust insulin dosages.
- Hyperlipidaemia due to the presence of lipids in the emulsion for infusion. Regular clinical and laboratory tests are required.
- Amino acid metabolism disorders

Special precautions in paediatrics

When administered to children greater than 2 years old, it is essential to use a bag which has a volume corresponding to the daily dosage.

Vitamin and trace element supplementation is always required. Paediatric formulations should be used.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed

Ceftriaxone must not be co-administered with calcium-containing IV solutions, because of the risk of precipitation of ceftriaxone-calcium salt.

Oliclinomel contains vitamin K, naturally present in lipid emulsions. The amount of Vitamin K in recommended doses of Oliclinomel are not expected to influence effects of coumarin derivatives.

This emulsion for infusion must not be administered simultaneously with blood through the same infusion tubing because of the possibility of pseudoagglutination.

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 have been eliminated (these are generally eliminated after a period of 5 to 6 hours without receiving lipids).

Due to the potassium content of OLICLINOMEL, special care should be taken in patients treated with potassium-saving diuretics (e.g, amiloride, spironolactone, triamterene) angiotensin converting enzyme (ACE) inhibitors, angiotensin II receptor antagonists or the immunosuppressants tacrolimus or cyclosporine in view of the risk of hyperkalemia.

4.6 Fertility, pregnancy and lactation

There are not at present sufficient relevant clinical findings to assess the tolerability of the ingredients in OliClinomel in women who are pregnant or breast-feeding.

In the absence of data, the prescriber must assess the risks / benefits before deciding to administer this emulsion either during pregnancy or to women who are breast-feeding.

4.7 Effects on ability to drive and use machines

There are no data on the effects of the ability to operate and automobile or other heavy machinery

4.8 Undesirable effects

Potential undesirable effects may occur as a result of inappropriate use (for example: overdose, excessively fast infusion rate) (see sections 4.4 and 4.9).

At the beginning of the infusion, any abnormal signs or symptoms of an allergic reaction (e.g. sweating, fever, shivering, headache, skin rashes, dyspnoea) should be cause for immediate discontinuation of the infusion.

OLICLINOMEL N4-550E, N7-1000E, and N8-800 have been used in three (3) clinical trials to evaluate the ease of use, safety and nutritional efficacy of the product.

One trial was a randomized, double-blind, active-controlled, efficacy and safety study conducted with OLICLINOMEL N8-800. Twenty-eight patients with various medical conditions (i.e., postsurgical fasting, severe malnutrition, enteral intake insufficient or forbidden) were included and treated; patients in the OLICLINOMEL group received drug product up to 40 mL/kg/d over 5 days.

The other two trials were open-label, non-comparative studies to evaluate the ease of use, safety and efficacy of OLICLINOMEL in gastrointestinal surgery patients. In these trials, a total of 36 patients received drug product up to 40 mL/kg/d over 5 days in OLICLINOMEL N4-550E study (N = 20), and up to 36 mL/kg/d over 5 days in OLICLINOMEL N7-1000E study (N = 16)

The pooled data (64 patients) from these 3 clinical trials and the postmarketing experience indicate the following adverse drug reactions (ADRs) related to OLICLINOMEL

System Organ Class (SOC)	Preferred MedDRA Term	Frequency[a]
IMMUNE SYSTEM DISORDERS	Hypersensitivity	common[b]
NERVOUS SYSTEM DISORDERS	Headache	common[b]
	Tremor	Not known[c]
GASTROINTESTINAL DISORDERS	Diarrhoea Abdominal pain Vomiting Nausea	common[b] Not known[c] Not known[c] Not known[c]
RENAL AND URINARY DISORDERS	Azotemia	common[b]
HEPATO-BILIARY DISORDERS	Hepatitis cholestatic Cholestasis Jaundice	Not known[c] Not known[c] Not known[c]
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	Erythema Hyperhydrosis	Not known[c] Not known[c]
MUSCULOSKELETAL, CONNECTIVE TISSUE AND BONE DISORDERS	Musculoskeletal pain Back pain Chest pain	Not known[c] Not known[c]

	Pain in extremity Muscle spasm	Not known[c] Not known[c] Not known[c]
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	Chills Infusion site extravasation Infusion site pain Infusion site swelling Infusion site vesicles Catheter site phlebitis Injection site edema Localized edema Edema peripheral Pyrexia Feeling hot Hyperthermia Malaise Inflammation	common[b] common[b] common[b] common[b] common[b] Not known[c] Not known[c] Not known[c] Not known[c] Not known[c] Not known[c] Not known[c] Not known[c] Not known[c]
INVESTIGATIONS	Blood bilirubin increased Hepatic enzyme increased Gamma-glutamyltransferase increased Blood triglycerides increased Blood alkaline phosphatase increased Blood glucose increased Hyperglycemia	Not known[c] common[b] common[b] common[b] common[b] Not known[c] Not known[c]

a: Frequency is defined as very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1000 to < 1/100): rare (≥ 1/10,000 to < 1/1000); very rare (< 1/10,000); and not known (cannot be estimated from the available data).
b: ADR reported during clinical trials. These studies included only 64 patients who were exposed to OLICLINOMEL.
c: ADR reported during postmarketing experience with OLICLINOMEL.

Fat Overload Syndrome (very rare)
Fat overload syndrome has been reported with similar products. Reduced ability to remove the lipids contained in OliClinomel may result in a "fat overload syndrome" which may be caused by overdose however, the signs and symptoms of this syndrome may also occur at the start of an infusion when the product is administered according to instructions.This syndrome is associated with a sudden deterioration in the patient's clinical condition and is characterised by hyperlipidaemia, fever, liver fatty infiltration, hepatomegaly, anaemia, leucopaenia, thrombocytopaenia, coagulation disorders, and coma, requiring hospitalization. These symptoms are reversible when the lipid emulsion infusion is stopped.

Pediatric population
Thrombocytopenia has been reported in children receiving lipid infusions.

4.9 Overdose

In the event of inappropriate administration (overdose and/or infusion rate higher than recommended), signs of hypervolaemia and acidosis may occur.

An excessively fast administration of Total Parenteral Nutrition (TPN) solutions, including OLICLINOMEL, may result in severe or fatal consequences. (See section 4.4 Special warning and precautions for use).

Hyperglycaemia, glucosuria, and a hyperosmolar syndrome may develop if excessive glucose is administered.

Excessively fast infusion or administration of an inappropriately large volume may cause nausea, vomiting, chills, and electrolyte disturbances. In such situations, the infusion should be stopped immediately.

A reduced ability to remove lipids may result in a "fat overload syndrome", the effects of which are usually reversible after the lipid infusion is stopped (see also section 4.8).

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

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Solutions for parenteral nutrition/mixtures ATC code: B05 BA 10.

This is a ternary mixture 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. In addition this formulation contains electrolytes.

The amino acid solution contains 15 L series amino acids (including 8 essential amino acids), which are indispensable for protein synthesis.

The amino acids also represent an energy source, their oxidation resulting in excretion of nitrogen in the form of urea.

The amino acid profile is as follows:
- Essential amino acids/total amino acids: 40.5%
- Essential amino acids (g)/total nitrogen (g): 2.5
- Branched-chain amino acids/total amino acids: 19%

The carbohydrate source is glucose***:*** (80 g/l)

The lipid emulsion 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 amount of alpha tocopherol which, combined with a moderate PUFA intake, contributes to improve vitamin E status and reduce lipid peroxidation.

5.2 Pharmacokinetic properties

The ingredients of the emulsion for infusion (amino acids, electrolytes, glucose, lipids) are distributed, metabolised and removed 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 vena porta 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.

The size of the lipid particles in the emulsion contained in OliClinomel is close to that of chylomicrons and this emulsion therefore has a similar elimination rate.

5.3 Preclinical safety data

No preclinical studies have been performed on the OliClinomel finished product.

Preclinical studies performed using the solutions of amino acids and glucose contained in OliClinomel of different qualitative compositions and concentrations have not, however, revealed any specific toxicity.

Preclinical toxicity studies performed using the lipid emulsion contained in OliClinomel have identified the changes, which are conventionally found with a high intake of a lipid emulsion: fatty liver, thrombocytopaenia and elevated cholesterol.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lipid emulsion compartment:

- Purified egg phosphatide
- Glycerol
- Sodium oleate
- Sodium hydroxide (for pH adjustment)
- Water for injections

Amino acid solution compartment:

- Glacial acetic acid (for pH adjustment)
- Water for injections

Glucose solution compartment:

- Hydrochloric acid (for pH adjustment)
- Water for injections

6.2 Incompatibilities

Do not add other medicinal products or substances to 1 of the 3 components of the bag or to the reconstituted emulsion without first confirming their compatibility and the stability of the resulting preparation (in particular the stability of the lipid emulsion).

Incompatibilities may be produced for example by excessive acidity (low pH) or inappropriate content of divalent cations (Ca^{2+} and Mg^{2+}), which may de-stabilise the lipid emulsion.

Calcium-containing IV solutions such as OLICLINOMEL must not be co-administered with ceftriaxone. (See section 4.5)

Check compatibility with solutions administered simultaneously through the same administration set, catheter or cannula.

Do not administer before, simultaneously with or after blood through the same equipment because of the risk of pseudoagglutination.

6.3 Shelf life

2 years if the overwrap is not damaged.

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

The reconstituted emulsion has, however, been shown to be stable for a maximum of 7 days at between +2° and +8°C followed by a maximum of 48 h at temperatures not exceeding + 25°C.

After addition of supplements (electrolytes, organic phosphate, trace elements, vitamins; *see section 6.6):*
For specific admixtures, chemical and physical in-use stability has been demonstrated for 7 days at 2 to 8°C followed by 48 hours below 25°C. From a microbiological point of view, any admixture should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8°C, unless addition of supplements has taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage

Do not freeze.

Keep container in the outer carton.

For storage of the reconstituted emulsion, *see section 6.3*

6.5 Nature and contents of container

The 3 compartment bag is a multi-layer plastic bag. The inner (contact) layer of the bag material 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 EVA (poly(ethylene-vinyl acetate)), and of a copolyester.

The bag is packaged in an oxygen barrier overwrap, which contains an oxygen absorber in a sachet.

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.

After the seals have been broken, the capacity of the bag is sufficient to enable vitamins, electrolytes and trace elements to be added.

PACK SIZES:

1000 ml in a 3 compartment bag (400 ml 5.5% amino acid solution (corresponding to 5.5g/100ml)+ 400 ml 20% glucose solution (corresponding to 20g/100ml) + 200 ml 10% lipid emulsion (corresponding to 10g/100ml)
Carton with 6 bags.

1000 ml in a 3 compartment bag (400 ml 5.5% amino acid solution (corresponding to 5.5g/100ml)+ 400 ml 20% glucose solution (corresponding to 20g/100ml) + 200 ml 10% lipid emulsion (corresponding to 10g/100ml)
1 bag.

1500 ml in a 3 compartment bag (600 ml 5.5% amino acid solution (corresponding to 5.5g/100ml)+ 600 ml 20% glucose solution (corresponding to 20g/100ml) + 300 ml 10% lipid emulsion (corresponding to 10g/100ml)
Carton with 4 bags.

1500 ml in a 3 compartment bag (600 ml 5.5% amino acid solution (corresponding to 5.5g/100ml)+ 600 ml 20% glucose solution (corresponding to 20g/100ml) + 300 ml 10% lipid emulsion (corresponding to 10g/100ml)
1 bag.

2000 ml in a 3 compartment bag (800 ml 5.5% amino acid solution (corresponding to 5.5g/100ml)+ 800 ml 20% glucose solution (corresponding to 20g/100ml) + 400 ml 10% lipid emulsion (corresponding to 10g/100ml)
Carton with 4 bags.

2000 ml in a 3 compartment bag (800 ml 5.5% amino acid solution (corresponding to 5.5g/100ml)+ 800 ml 20% glucose solution (corresponding to 20g/100ml) + 400 ml 10% lipid emulsion (corresponding to 10g/100ml)
1 bag.

2500 ml in a 3 compartment bag (1000 ml 5.5% amino acid solution (corresponding to 5.5g/100ml)+ 1000 ml 20% glucose solution (corresponding to 20g/100ml) + 500 ml 10% lipid emulsion (corresponding to 10g/100ml)
Carton with 2 bags.

2500 ml in a 3 compartment bag (1000 ml 5.5% amino acid solution (corresponding to 5.5g/100ml)+ 1000 ml 20% glucose solution (corresponding to 20g/100ml) + 500 ml 10% lipid emulsion (corresponding to 10g/100ml)
1 bag.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

a. *To open*

- Tear the protective overwrap.
- When present, discard the oxygen absorber sachet after removing the overwrap.
- 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) and if the amino acids solution and the glucose solution are clear, colorless, 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 ambient 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 half of their length. Mix by inverting the bag at least 3 times.

c. *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.

d. *Additions*

The capacity of the bag is sufficient to enable additions such as, vitamins, electrolytes, and trace elements**.** Any additions (including vitamins) may be made into the reconstituted mixture (after the non-permanent seals have been opened and the contents of the three compartments have been mixed).

Vitamins may also be added into the glucose compartment before the mixture has been reconstituted (before opening the non-permanent seals and before mixing the solutions and the emulsion).

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

Oliclinomel may be supplemented with:

- Electrolytes: electrolytes already present in the bag should be taken into account: stability has been demonstrated up to a total quantity of 150 mmol of sodium, 150 mmol of potassium, 5.6 mmol of magnesium and 5 mmol of calcium per litre of the ternary mixture.
- Organic phosphate: stability has been demonstrated for additions of up to 15 mmol per bag.
- 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.

Additions must be performed by qualified personnel under aseptic conditions.

These additions are made into the injection site using a needle:
- Prepare the injection site,
- Puncture the injection site and inject,
- Mix the contents of the bag and the additives.

e. *Administration*

For single use only.

Only administer the product after the non-permanent seals between the 3 compartments have been broken and the contents of the 3 compartments have been mixed.
Ensure that the final emulsion for infusion does not show any evidence of phase separation.

After opening the bag, the contents must be used immediately. The opened bag must never be stored for a subsequent infusion.

Do not reconnect any partially used bag.

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

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

Do not store any partially used bags and discard all devices after use

7 MARKETING AUTHORISATION HOLDER

Baxter Healthcare Ltd.
Caxton Way
Thetford
Norfolk
IP24 3SE
UK

8 MARKETING AUTHORISATION NUMBER

PA 0167/109/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

March 2012