Lipid Emulsion + Amino Acids + Electrolytes + Glucose

Combiflex® Lipid Peri

Emulsion for I.V. Infusion
PARENTERAL NUTRITION

FORMULATION
Lipid Emulsion/Amino Acids/Electrolytes/Glucose (Combiflex®Lipid Peri) is available in a three chamber bag system. Each bag contains different volumes depending on the pack sizes.

	1920 mL	**1440 mL**	**384 mL**
Glucose 11% Solution	1180 mL	885 mL	236 mL
Amino acids 11.3% Solution with Electrolytes	400 mL	300 mL	80 mL
Lipid 20% Emulsion	340 mL	255 mL	68 mL

Active Ingredients	1920mL	1440mL	384mL
Purified soya oil	68 g	51 g	13.60 g
Glucose monohydrate	143 g	107g	28.556 g
- corresponding to Glucose (anhydrous)	130 g	97 g	25.96 g
Alanine	6.4 g	4.8 g	1.28 g
Arginine	4.5 g	3.4g	0.904 g
Aspartic acid	1.4 g	1 g	0.272 g
Glutamic acid	2.2 g	1.7 g	0.448 g
Glycine	3.2 g	2.4 g	0.632 g
Histidine	2.7 g	2 g	0.655 g
Isoleucine	2.2 g	1.7 g	0.448 g
Leucine	3.2 g	2.4 g	0.632 g
Lysine hydrochloride	4.5 g	3.4 g	0.904 g
- corresponding to Lysine	3.6 g	2.7 g	(0.723 g)
Methionine	2.2 g	1.7 g	0.448 g
Phenylalanine	3.2 g	2.4 g	0.632 g
Proline	2.7 g	2 g	0.544 g
Serine	1.8 g	1.4 g	0.360 g
Threonine	2.2 g	1.7 g	0.448 g
Tryptophan	0.76 g	0.57 mg	0.152 g
Tyrosine	0.092 g	0.069 mg	0.018 g
Valine	2.9 g	2.2 g	0.584 g
Calcium chloride dihydrate	0.39 g	0.29 mg	0.078 g
- corresponding to Calcium chloride	0.30 g	0.22 mg	(0.059 g)
Sodium glycerophosphate hydrate	2.9 g	2.1 g	0.571 g
- corresponding to Sodium glycerophospate, anhydrous	2 g	1.5 g	(0.403 g)
Magnesium sulphate heptahydrate	1.3 g	0.99 mL	0.263 g
- corresponding to Magnesium sulfate	0.64 g	0.48 mL	(0.128 g)
Potassium chloride	2.4 g	1.8 g	0.478 g
Sodium acetate trihydrate	3.3 g	2.5 g	0.654 g
- corresponding to Sodium acetate	2 g	1.5 g	(0.392 g)
• Amino acids	45 g	34 g	9 g
• Nitrogen	7.2 g	5.4 g	1.4 g
• Lipid	68 g	51 g	13.6 g
• Carbohydrates			
- Glucose (dextrose)	130 g	97 g	26 g
• Calorie content			
- total	1400 kcal	1000 kcal	267 kcal
- non protein	1200 kcal	900 kcal	240 kcal
• Electrolytes			
- sodium	43 mmol	32 mmol	8.5 mmol
- potassium	32 mmol	24 mmol	6.4 mmol
- magnesium	5.3 mmol	4 mmol	1.1 mmol
- calcium	2.7 mmol	2 mmol	0.5 mmol
- phosphate	14 mmol	11 mmol	2.9 mmol
- sulfate	5.3 mmol	4 mmol	1.1 mmol
- chloride	62 mmol	47 mmol	12.5 mmol
- acetate	52 mmo	39 mmol	10.4 mmol
• Osmolality	approx. 830 mOsm/Kg water		
• Osmolarity	approx. 750 mOsm/L		
• pH	approx. 5.6		

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

DOSAGE AND ADMINISTRATION
The dose should be individualized and the choice of bag size should be made with regard to patient's clinical condition, body weight and nutritional requirements.

Adult patients
The nitrogen requirements for maintenance of body protein mass depend on the patient's condition (e.g. nutritional state and degree of catabolic stress). The requirements are 0.1-0.15 g nitrogen/Kg body weight/day in the normal nutritional state. In patients with moderate to high metabolic stress with or without malnutrition, the requirements are in the range of 0.15-0.3g nitrogen/Kg body weight/day (1-2 amino acid/Kg body weight/day). The corresponding commonly accepted requirements are 2-6 g for glucose and 1-2g for lipid.

The dosage range of 0.10-0.15g nitrogen/Kg body weight/day (0.7-1.0 g amino acid/Kg body weight/day) and a total energy of 20-30 kcal body weight/day corresponds to approx. 27-40 mL/Kg body weight per day.

The total energy requirement depends on the patient's clinical condition and is often between 20-30 kcal/Kg body weight/day. In obese patients the dose should be based on the estimated ideal weight.

Lipid Emulsion/Amino Acids/Electrolytes/Glucose (Combiflex® Lipid Peri) is produced in two sizes intended for patients with moderately increased, basal or low nutritional requirements. To provide total parenteral nutrition, the addition of trace elements, vitamins and supplemental electrolytes may be required.

Children
The ability to metabolize individual nutrients must determine the dosage.

In general the infusion for small children (2-10 years) should start with a low dose i.e. 14-28 mL/Kg (corresponding to 0.49-0.98 g lipid/Kg/day, 0.34-0.67 g amino acids/Kg/day and 0.95-1.9 g glucose/Kg/day) and increased by 10-15 mL/Kg/day up to maximum dosage of 40 mL/Kg/day.

For children over 10 years of age the dosage for adults can be applied. The use of Lipid Emulsion/Amino Acids/ Electrolytes/Glucose (Combiflex®Lipid Peri) is not recommended in children under 2 years of age in whom the amino acid cysteine may be considered conditionally essential.

Infusion rate
The maximum infusion rate for glucose is 0.25 g/Kg body weight/h. Amino acid dosage should not exceed 0.1 g/Kg body weight/h. Lipid dosage should not provide more than 0.15 g/Kg body weight/h.

The infusion rate should not exceed 3.7 mL/Kg body weight/h (corresponding to 0.25 g glucose, 0.09 g amino acids, 0.13 g lipid per Kg body weight). The recommended infusion period for individual bags of Lipid Emulsion/Amino Acids/ Electrolytes/Glucose (Combiflex®Lipid Peri) is 12-24 hours. Intravenous infusion into a peripheral or central vein. Infusion may be continued for as long as required by the patient's clinical condition. In order to minimize the risk of thrombophlebitis for peripheral application, daily rotation of infusion site is recommended.

DIRECTION FOR USE AND HANDLING

For single use only
Do not use if package is damaged. The contents of the 3 separate chamber bag should be freshly mixed prior to use. The mixed emulsion is for single use only. Remove the outer wrap. Break the partition by rolling the hanger part. After separation of the peelable seals, the bag should be inverted to several occasions or shake well to blend the solution of amino acids, glucose and lipid uniformly until a homogenous mixture is produced.

Use the product if the amino acids and glucose solutions are clear and colourless or slightly yellow and if the lipid solution is white and homogenous. Only medicinal or nutritional solutions for which compatibility has been documented may be added to Lipid Emulsion/Amino Acids/ Electrolytes/Glucose (Combiflex®Lipid Peri). Addition should be made aseptically. Mixing data are delivered upon request. Discard the remaining mixture after infusion.

CONTRAINDICATIONS
Hypersensitivity to egg, soya or peanut protein or to any of the active substances or excipients
Severe hyperlipaemia
Severe liver insufficiency
Severe blood coagulation disorders
Inborn errors of amino acids metabolism
Severe renal insufficiency without access to hemofiltration or dialysis
Acute shock
Hyperglycemia, which requires more than 6 units insulin/h
Pathologically elevated serum levels of any of the included electrolytes.
General contraindications to infusion therapy: acute pulmonary edema, hyper hydration and decompensated cardiac insufficiency and hypotonic dehydration.
Haemophagocytotic syndrome
Unstable conditions (e.g. severe post-traumatic conditions, uncompensated diabetes, acute myocardial infarction, metabolic acidosis, severe sepsis and hyperosmolar coma).
Infants under 2 years of age.

WARNINGS AND PRECAUTIONS
The ability to eliminate lipid should be monitored. It is recommended that this is done by measuring serum triglycerides after a lipid-free period of 5-6 hours. The serum concentration of triglycerides should not exceed 3 mmol/L during infusion. The bag size, especially the volume and the quantitative composition, should be carefully chosen. These volumes should be adjusted according to the hydration and nutritional status of the children. One reconstituted bag is for single use. Disturbances of the electrolyte and fluid balance (e.g. abnormally high or low serum levels of the electrolytes) should be corrected before starting the infusion. Special clinical monitoring is required at the beginning of any intravenous infusion. Should any abnormal sign occur, the infusion must be stopped. Since an increased risk of infection is associated with the use of any central vein, strict aseptic precautions should be taken to avoid any contamination during catheter insertion and manipulation. Lipid Emulsion/Amino Acids/Electrolytes/Glucose (Combiflex® Lipid Peri) should be given with caution in conditions of impaired lipid metabolism due to renal insufficiency, uncompensated diabetes mellitus, pancreatitis, impaired liver function, hypothyroidism (with hypertriglyceridaemia) or sepsis. If Lipid Emulsion/Amino Acids/ Electrolytes/Glucose (Combiflex®Lipid Peri) is given to patients with these conditions, close monitoring of serum triglyceride concentrations is mandatory. Serum glucose, electrolytes and osmolarity as well as fluid balance, acid-base status and liver enzyme tests should be regularly monitored. Blood cell count and coagulation should be monitored when lipid is given for a longer period. In patients with renal insufficiency, the phosphate and potassium intake should be carefully controlled to prevent hyperphosphataemia and hyperkalemia.The amount of supplemental electrolytes should be determined by regular monitoring taking into consideration the clinical condition of the patient. This emulsion is free of vitamins and trace-elements. The addition of trace elements and vitamins is always required. Parenteral nutrition should be given with caution to patients with metabolic acidosis (e.g. lactic acidosis), increased serum osmolarity or those in need of fluid resuscitation. Lipid Emulsion/Amino Acids/ Electrolytes/Glucose (Combiflex®Lipid Peri) should be given with caution to patients with a tendency towards electrolyte retention. Any sign or symptom of anaphylactic reaction(such as fever, shivering, rash or dyspnea) necessitates immediate interruption of the infusion. The lipid content of Lipid Emulsion/Amino Acids/ Electrolytes/Glucose (Combiflex® Lipid Peri) may interfere with certain laboratory measurements (e.g. bilirubin, lactate dehydrogenase, oxygen saturation, hemoglobin) if blood is sampled before lipid has been adequately cleared from the bloodstream. Lipid is cleared after a lipid-free interval of 5-6 hours in most patients. This medicinal product contains soya-bean oil and egg phospholipids, which may rarely cause allergic reactions. Cross allergic reaction has been observed between soya-bean and peanut.
Intravenous infusion of amino acids may be accompanied by increased urinary excretion of trace elements, particularly zinc. Additional supplements of trace elements may be required in patients requiring long-term intravenous nutrition. In malnourished patients, initiation of parenteral nutrition can precipitate fluid shifts resulting in pulmonary oedema and congestive heart failure. In addition, decreases in the serum concentrations of potassium, phosphorus, magnesium and water soluble vitamins may occur within 24 to 48 hours. Careful and slow initiation of parenteral nutrition is recommended together with close monitoring and appropriate adjustments of fluid, electrolytes, minerals and vitamins.

Lipid Emulsion/Amino Acids/ Electrolytes/Glucose (Combiflex®Lipid Peri) should not be given simultaneously with blood or blood products in the same infusion set. In patients with hyperglycemia, administration of exogenous insulin might be necessary.

Peripheral Infusion
As with all hypertonic solutions, thrombophlebitis may occur if peripheral veins are used for infusions. Several factors contribute to the incidence of thrombophlebitis. These include the type of cannula used and its diameter and length, the duration of infusion, pH and osmolality of infusates, infection and the number of manipulations. It is recommended that venous access sites for Total Parenteral Nutrition should not be used for other intravenous additives or solutions.

PREGNANCY AND LACTATION
No specific studies have been performed to assess the safety of Lipid Emulsion/Amino Acids/ Electrolytes/Glucose (Combiflex®Lipid Peri) in pregnancy and lactation. The prescriber should consider the benefit/risk relationship before administering Lipid Emulsion/Amino Acids/ Electrolytes/Glucose (Combiflex®Lipid Peri) to pregnant or breast feeding women.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINE
Not applicable

UNDESIRABLE EFFECTS
The infusion may cause a rise in body temperature (incidence<3%) and, less frequently, shivering, chills and nausea/vomiting (incidence<1%). Transient increases in liver enzymes during intravenous nutrition have also been reported. As with all hypertonic solutions for infusion, thrombophlebitis may occur if peripheral veins are used.

Reports of the undesirable effects in conjunction with the included components are extremely rare. Hypersensitivity reactions (anaphylactic reaction, skin rash, urticaria), respiratory symptoms (e.g. tachypnoea) and hyper / hypotension have been described. Haemolysis, reticulocytosis, abdominal pain, headache, nausea, vomiting, tiredness and priapism have been reported.

Lipid overload syndrome
An impaired capacity to eliminate lipid may lead to the lipid overload syndrome. This may occur as a result of overdosage, but also at recommended rates of infusion, in association with a sudden change in the patient's clinical condition resulting in severe renal or hepatic impairment.

The lipid overload syndrome is characterized by hyperlipidaemia, fever, hepatosplenomegaly, anaemia, leucopenia, thrombocytopenia, coagulopathies and coma. These changes are invariably reversible on discontinuation of the lipid infusion.

OVERDOSE
Nausea, vomiting and sweating have been observed during infusion of amino acids at rates exceeding the recommended maximum rate.

If symptoms of overdose occur, the infusion should be slowed down or discontinued.

Additionally, overdose might cause fluid overload, electrolyte imbalances, hyperglycemia, and hyperosmolality.

In some rare serious cases, haemodialysis, haemofiltration or haemo-diafiltration may be necessary.

CAUTION
Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

STORAGE CONDITION
Store at temperatures not exceeding 30°C. Do not freeze.
Store in over pouch provided. After breaking the seals, chemical and physical in-use stability of the mixed three chamber bag has been demonstrated for 24 hours at 30°C.

AVAILABILITY
384mL capacity 3-chamber bag (box of 8's)
1920mL capacity 3-chamber bag (box of 2's)
1440mL capacity chamber bag (box of 4's)

Manufactured by
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