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Directions for Use

B. Braun Melsungen AG · 34209 Melsungen, Germany

Glucose + Amino Acids + Lipids

NuTRIflex® Lipid peri

Emulsion for infusion
Total Parenteral Nutrition

Formulation
The ready to use emulsion for infusion contains after mixing of the contents of the individual chambers:

Active ingredients

– from the upper, left chamber	**in 1250 mL**	**in 1875 mL**	**in 2500 mL**
Glucose monohydrate	88.0 g	132.0 g	176.0 g
equivalent to anhydrous glucose	80.0 g	120.0 g	160.0 g
Sodium dihydrogen phosphate dihydrate	1.170 g	1.755 g	2.340 g
Zinc acetate dihydrate	6.625 mg	9.9 mg	13.2 mg
– from the upper, right chamber	**in 1250 mL**	**in 1875 mL**	**in 2500 mL**
Soya-bean oil	25.0 g	37.5 g	50.0 g
Medium-chain triglycerides	25.0 g	37.5 g	50.0 g
– from the lower chamber	**in 1250 mL**	**in 1875 mL**	**in 2500 mL**
Isoleucine	2.34 g	3.51 g	4.68 g
Leucine	3.13 g	4.70 g	6.26 g
Lysine hydrochloride	2.84 g	4.26 g	5.68 g
eq. to Lysine	2.26 g	3.39 g	4.52 g
Methionine	1.96 g	2.94 g	3.92 g
Phenylalanine	3.51 g	5.27 g	7.02 g
Threonine	1.82 g	2.73 g	3.64 g
Tryptophan	0.57 g	0.86 g	1.14 g
Valine	2.60 g	3.90 g	5.20 g
Arginine	2.70 g	4.05 g	5.40 g
Histidin hydrochloride monohydrate	1.69 g	2.54 g	3.38 g
eq. to Histidine	1.25 g	1.88 g	2.50 g
Alanine	4.85 g	7.28 g	9.70 g
Aspartic acid	1.50 g	2.25 g	3.00 g
Glutamic acid	3.50 g	5.25 g	7.00 g
Glycine	1.65 g	2.48 g	3.30 g
Proline	3.40 g	5.10 g	6.80 g
Serine	3.00 g	4.50 g	6.00 g
Sodium hydroxide	0.800 g	1.200 g	1.600 g
Sodium chloride	1.081 g	1.622 g	2.162 g
Sodium acetate trihydrate	0.544 g	0.816 g	1.088 g
Potassium acetate	2.943 g	4.415 g	5.886 g
Magnesium acetate tetrahydrate	0.644 g	0.966 g	1.288 g
Calcium chloride dihydrate	0.441 g	0.662 g	0.882 g
Amino acid content [g]	40	60	80
Total nitrogen content [g]	5.7	8.6	11.4
Carbohydrate content [g]	80	120	160
Lipid content [g]	50	75	100
Energy in the form of lipid [kJ/(kcal)]	1990 (475)	2985 (715)	3980 (950)
Energy in the form of carbohydrate [kJ/(kcal)]	1340 (320)	2010 (480)	2680 (640)
Energy in the form of amino acids [kJ/(kcal)]	670 (160)	1005 (240)	1340 (320)
Non-protein energy [kJ/(kcal)]	3330 (795)	4995 (1195)	6660 (1590)
Total energy [kJ/(kcal)]	4000 (955)	6000 (1435)	8000 (1910)
Osmolality [mOsm/kg]	920	920	920
pH	5.0 - 6.0	5.0 - 6.0	5.0 - 6.0
Electrolyte content (mmol)			
Sodium	50	75	100
Potassium	30	45	60
Magnesium	3.0	4.5	6.0
Calcium	3.0	4.5	6.0
Zinc	0.03	0.045	0.06
Chloride	48	72	96
Acetate	40	60	80
Phosphate	7.5	11.25	15

Excipients:
Citric acid monohydrate, egg lecithin, glycerol, sodium oleate, water for injections

Pharmacologic Category
Emulsion for intravenous supply of amino acids, carbohydrates, fat and electrolytes.

Indications
Supply of the daily requirement of energy, essential fatty acids, amino acids, electrolytes and fluids during parenteral nutrition for patients with mild to moderately severe catabolism when oral or enteral nutrition is impossible, insufficient or contraindicated.

Contraindications
This product must not be administered in the following conditions
- disturbances of amino acid metabolism,
- disturbances of lipid metabolism,
- hyperkalaemia; hyponatraemia,
- unstable metabolism (e.g. severe postaggression syndrome, unstabilized diabetic metabolic situation, coma of unknown origin),
- hyperglycaemia not responding to insulin doses of up to 6 units insulin/hour,
- acidosis,
- intrahepatic cholestasis,
- severe hepatic insufficiency,
- severe renal insufficiency,
- manifest cardiac insufficiency,
- aggravating haemorrhagic diatheses,
- acute phases of cardiac infarction and stroke,
- acute thrombo-embolic events, lipid embolism.
- known hypersensitivity to egg or soya-bean protein or to any of the ingredients

On account of its composition NuTRIflex® Lipid peri should not be used for neonates, infants and children under 2 years of age.

General contra-indications to parenteral nutrition are:
- unstable circulatory status with vital threat (states of collapse and shock),
- inadequate cellular oxygen supply,
- states of hyperhydration,
- disturbances of the electrolyte and fluid balance, acute pulmonary oedema, decompensated cardiac insufficiency

Pregnancy and Lactation
NuTRIflex® Lipid peri should only be used in pregnancy if there is an imperative indication. This medicine manufactured with soya-bean oil contains phytosterols in concentrations that could lead to disturbances of fertility, according to results of testing of the purified substance in animal experiments. At present there are no studies available making a risk-benefit assessment possible with regard to effects on the embryo or the fetus.
Breast-feeding is not recommended if women need parenteral nutrition in that time.

Special Warnings and Special Precautions for Use
Caution should be exercised in cases of increased serum osmolarity.
As for all large-volume infusion solutions NuTRIflex® Lipid peri should be administered with caution to patients with impaired cardiac or renal function. Disturbances of the fluid, electrolyte or acid-base balance, e.g. hyperhydration, hyperkalaemia, acidosis, should be corrected before the start of infusion. Too rapid infusion can lead to fluid overload with pathological serum electrolyte concentrations, hyperhydration and pulmonary oedema.
The serum triglyceride concentration should be monitored when infusing NuTRIflex® Lipid peri. Fasting lipaemia should be excluded in patients with suspected disturbances of lipid metabolism before starting infusion. The administration of lipids is contraindicated if there is fasting lipaemia. The presence of hypertriglyceridaemia 12 hours after lipid administration also indicates a disturbance of lipid metabolism
NuTRIflex® Lipid peri should be administered cautiously to patients with disturbances of lipid metabolism, e.g. renal insufficiency, diabetes mellitus, pancreatitis, impaired hepatic function, hypothyroidism (with hypertriglyceridemia) and sepsis. If NuTRIflex® Lipid peri is given to patients with these conditions, close monitoring of serum triglycerides is mandatory.
Any sign or symptom of anaphylactic reaction (such as fever, shivering, rash or dyspnoea) should lead to immediate interruption of the infusion.
Depending on the patient´s metabolic condition, occasional hypertriglyceridaemia or increases of the blood glucose concentration may occur. If the plasma triglyceride concentration rises to more than 3 mmol/l during administration of lipid it is recommen-

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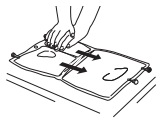
ded that the infusion rate should be reduced. Should the plasma triglyceride concentration remain above 3 mmol/l the administration should be stopped until the level normalizes.
A dose reduction or interruption of administration is also indicated if the blood glucose concentration rises to more than 14 mmol/l (250 mg/dl) when administering the lipid.
As with all solutions containing carbohydrates the administration of NuTRIflex® Lipid peri can lead to hyperglycaemia. The blood glucose level should be monitored. If there is hyperglycaemia the rate of infusion should be reduced or insulin should be administered.
Intravenous infusion of amino acids is accompanied by increased urinary excretion of the trace elements, especially copper and, in particular, zinc. This should be considered in the dosing of trace elements, especially during longterm intravenous nutrition.
NuTRIflex® Lipid peri should not be given simultaneously with blood in the same infusion set due to the risk of pseudoagglutination.
Moreover controls of the serum ionogramme, the water balance, the acid-base balance and – during long-term administration - of blood cell counts, coagulation status and hepatic function are necessary.
The fat content may interfere with certain laboratory measurements (e.g. bilirubin, lactate dehydrogenase, oxygen saturation). If blood is sampled before fat has been adequately cleared from the blood stream.
Substitution of electrolytes, vitamins and trace elements may be necessary as required.
As NuTRIflex® Lipid peri contains zinc and magnesium, care should be taken when it is coadministered with solutions containing these elements.
As with all intravenous solutions strict aseptic precautions are necessary for the infusion of NuTRIflex® Lipid peri.
NuTRIflex® Lipid peri is a preparation of complex composition. It is, therefore, strongly advisable not to add other solutions.

Interactions
Some drugs, like insulin, may interfere with the body's lipase system. This kind of interaction seems, however, to be of only limited clinical importance.
Heparin given in clinical doses causes a transient release of lipoprotein lipase into the circulation. This may result initially in increased plasma lipolysis followed by a transient decrease in triglyceride clearance.
Soya-bean oil has a neutral content of vitamin K_1. This may interfere with the therapeutic effect of coumarin derivatives which should be closely monitored in patients treated with such drugs.

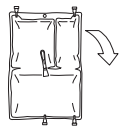
Dosage
The dosage is adapted to the individual patients' requirements.
The maximum daily dose is 40 mL per kg body weight, corresponding to
– 1.28 g amino acids /kg body weight per day
– 2.56 g glucose /kg body weight per day
– 1.6 g fat /kg body weight per day
It is recommended that NuTRIflex® Lipid peri be administered continuously. A stepwise increase of the infusion rate over the first 30 minutes up to the desired infusion rate avoids possible complications.
The maximum infusion rate is 2.5 mL/kg body weight per hour, corresponding to
– 0.08 g amino acids /kg body weight per hour
– 0.16 g glucose /kg body weight per hour
– 0.1 g fat /kg body weight per hour
For a patient weighing 70 kg this corresponds to an infusion rate of 175 mL/ kg body weight per hour. The amount of amino acid administered is then 5.6 g/hour, of glucose 11.2 g/hour and of lipid 7 g/ hour.

Method of administration
For intravenous infusion. Especially suitable for infusion into peripheral veins.

Preparation of the mixed solution:
Remove the bag from its protective pack and proceed as follows:
- open out the bag and lay on a solid surface
- open the peel seals to the two upper chambers by using pressure with both hands
- briefly mix the contents of the bag together



Preparation for infusion:
- fold the two empty chambers backwards
- hang the mixing bag on the infusion stand by the centre hanging loop
- remove the protective cap from the run-out port and carry out infusion using the normal technique



Duration of use
The duration of treatment for the indications stated should not exceed 7 days.

Overdose
Overdose of NuTRIflex® Lipid peri is not to be expected on proper administration.

Symptoms of fluid and electrolyte overdose
Hypertonic hyperhydration, electrolyte imbalance and pulmonary oedema.

Symptoms of amino acid overdose:
Renal amino acid losses with consecutive amino acid imbalances, sickness, vomiting and shivering.

Symptoms of glucose overdose:
Hyperglycaemia, glucosuria, dehydration, hyperosmolality, hyperglycaemic and hyperosmolar coma.

Symptoms of fat overdose:
Lipid overdose may lead to the overload syndrome, characterised (for example) by fever, headache, abdominal pain, fatigue, hyperlipaemia, hepatomegaly with or without jaundice, splenomegaly, pathological disturbances of liver function, anaemia, reduction in platelet count, reduction in white cell count, haemorrhagic diathesis and haemorrhage, alteration or depression of blood coagulation factors (bleeding time, coagulation time, prothrombin time etc.). The plasma triglyceride concentration should not exceed 3 mmol/l during infusion.

Emergency treatment, antidotes:
Immediate cessation of infusion is indicated for overdose. Further therapeutic measures depend on the particular symptoms and their severity. When infusion is recommenced after the symptoms have declined it is recommended that the infusion rate be raised gradually with monitoring at frequent intervals.

Undesirable effects
Possible early reactions on the administration of lipid emulsions are: slight increase in temperature, flush, cold feeling, shivering, loss of appetite, nausea, vomiting, respiratory distress, headache, pain in the back, bones, chest and lumbar region, fall or increase in blood pressure (hypotension, hypertension), hypersensitivity reactions (e.g. anaphylactic reactions, dermal eruptions).
Hot flushes or bluish discoloration of the skin due to reduced oxygen content of the blood (cyanosis) can occur as side effects.
If these side effects occur the infusion should be discontinued or, if appropriate, the infusion should be continued at a lower dose level.
Attention should be paid to the possibility of an overloading syndrome. This can occur as a result of individually varying, genetically determined metabolic conditions and can occur at different rates and after differing doses depending on previous disorders.
Overloading syndrome is associated with the following symptoms: enlargement of the liver (hepatomegaly) with and without jaundice (icterus), enlargement of the spleen (splenomegaly), fatty infiltration of the organs, pathological hepatic function parameters, anaemia, reduction of white cell count (leucopenia), reduction of platelet count (thrombocytopenia), a tendency to haemorrhage and haemorrhages, alterations or reduction in the blood coagulation factors (bleeding time, coagulation time, prothrombin time etc.), fever, hyperlipaemia, headache, stomache ache, fatigue.
If signs of vein wall irritation, phlebitis, or thrombophlebitis occur, change of the infusion site should be considered.
Please inform your doctor or pharmacist if you notice any undesirable effect that is not mentioned in this leaflet.

Caution
Foods, Drugs, Devices & Cosmetic Act prohibits dispensing without prescription.

Expiry date
The product must not be used beyond the expiry date stated on the labelling.

Instructions for storage / use / handling
Do not use after the product has passed the expiry date.
The emulsion is to be used immediately after mixing. It can be stored at 2 – 8 °C over 4 days, plus 48 hours at 25 °C.
Protect from light and store at temperatures not exceeding 25°C.
Do not freeze! If accidentally frozen, discard the bag.

Availability
Emulsion for intravenous infusion in three-chamber bags containing 1250 mL, 1875 mL and 2500 mL.

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34209 Melsungen, Germany

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