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Directions for Use

B. Braun Melsungen AG · 34209 Melsungen, Germany

Nutriflex® Omega special emulsion for infusion

Composition

The ready-for-use emulsion for intravenous infusion contains after mixing the chamber contents:

Active substances:

from the upper, left-hand chamber (glucose solution)	in 1000 ml	in 625 ml	in 1250 ml	in 1875 ml	in 2500 ml
Glucose monohydrate	158.4 g	99.0 g	198.0 g	297.0 g	396.0 g
equivalent to anhydrous glucose	144.0 g	90.0 g	180.0 g	270.0 g	360.0 g
Sodium dihydrogen phosphate dihydrate	2.496 g	1.56 g	3.120 g	4.680 g	6.240 g
Zinc acetate dihydrate	7.02 mg	4.39 mg	8.78 mg	13.17 mg	17.56 mg

from the upper, right-hand chamber (fat emulsion)	in 1000 ml	in 625 ml	in 1250 ml	in 1875 ml	in 2500 ml
Medium-chain triglycerides	20.0 g	12.5 g	25.0 g	37.5 g	50.0 g
Soya-bean oil refined	16.0 g	10.0 g	20.0 g	30.0 g	40.0 g
Omega-3-acid triglycerides	4.0 g	2.5 g	5.0 g	7.5 g	10.0 g

from the lower chamber (amino acid solution)	in 1000 ml	in 625 ml	in 1250 ml	in 1875 ml	in 2500 ml
Isoleucine	3.28 g	2.06 g	4.11 g	6.16 g	8.21 g
Leucine	4.38 g	2.74 g	5.48 g	8.22 g	10.96 g
Lysine hydrochloride	3.98 g	2.49 g	4.98 g	7.46 g	9.95 g
equivalent to Lysine	3.18 g	1.99 g	3.98 g	5.96 g	7.95 g
Methionine	2.74 g	1.71 g	3.42 g	5.13 g	6.84 g
Phenylalanine	4.92 g	3.08 g	6.15 g	9.22 g	12.29 g
Threonine	2.54 g	1.59 g	3.18 g	4.76 g	6.35 g
Tryptophan	0.80 g	0.50 g	1.00 g	1.50 g	2.00 g
Valine	3.60 g	2.26 g	4.51 g	6.76 g	9.01 g
Arginine	3.78 g	2.37 g	4.73 g	7.09 g	9.45 g
Histidine hydrochloride monohydrate	2.37 g	1.48 g	2.96 g	4.44 g	5.92 g
equivalent to Histidine	1.75 g	1.10 g	2.19 g	3.29 g	4.38 g
Alanine	6.79 g	4.25 g	8.49 g	12.73 g	16.98 g
Aspartic acid	2.10 g	1.32 g	2.63 g	3.94 g	5.25 g
Glutamic acid	4.91 g	3.07 g	6.14 g	9.20 g	12.27 g
Glycine	2.31 g	1.45 g	2.89 g	4.33 g	5.78 g
Proline	4.76 g	2.98 g	5.95 g	8.93 g	11.90 g
Serine	4.20 g	2.63 g	5.25 g	7.88 g	10.50 g
Sodium hydroxide	1.171 g	0.732 g	1.464 g	2.196 g	2.928 g
Sodium chloride	0.378 g	0.237 g	0.473 g	0.710 g	0.946 g
Sodium acetate trihydrate	0.250 g	0.157 g	0.313 g	0.470 g	0.626 g
Potassium acetate	3.689 g	2.306 g	4.611 g	6.917 g	9.222 g
Magnesium acetate tetrahydrate	0.910 g	0.569 g	1.137 g	1.706 g	2.274 g
Calcium chloride dihydrate	0.623 g	0.390 g	0.779 g	1.168 g	1.558 g

	in 1000 ml	in 625 ml	in 1250 ml	in 1875 ml	in 2500 ml
Amino acid content [g]	57.4	35.9	71.8	107.7	143.6
Total nitrogen content [g]	8	5	10	15	20
Carbohydrate content [g]	144	90	180	270	360
Lipid content [g]	40	25	50	75	100

Electrolyte concentration (mmol)					
Sodium	53.6	33.5	67	100.5	134
Potassium	37.6	23.5	47	70.5	94
Magnesium	4.24	2.65	5.3	7.95	10.6
Calcium	4.24	2.65	5.3	7.95	10.6
Zinc	0.03	0.02	0.04	0.06	0.08
Chloride	48	30	60	90	120
Acetate	48	30	60	90	120
Phosphate	16	10	20	30	40

Excipients:

Citric acid monohydrate, egg lecithin, glycerol, sodium oleate, all-rac-α-tocopherol, sodium hydroxide (for pH adjustment) and water for injections

Pharmaceutical form

Emulsion for infusion
Infusion bag with three compartments containing 625 ml, 1250 ml, 1875 ml or 2500 ml

Amino acids and glucose solutions: clear, colourless up to faintly straw-coloured solutions
Lipid emulsion: white, milky oil-in-water emulsion

	in 1000 ml	in 625 ml	in 1250 ml	in 1875 ml	in 2500 ml
Energy in the form of lipid [kJ (kcal)]	1592 (380)	995 (240)	1990 (475)	2985 (715)	3980 (950)
Energy in the form of carbohydrate [kJ (kcal)]	2412 (576)	1510 (360)	3015 (720)	4520 (1080)	6030 (1440)
Energy in the form of amino acids [kJ (kcal)]	936 (224)	585 (140)	1170 (280)	1755 (420)	2340 (560)
Non-protein energy [kJ (kcal)]	4004 (956)	2505 (600)	5005 (1195)	7510 (1795)	10010 (2390)
Total energy [kJ (kcal)]	4940 (1180)	3090 (740)	6175 (1475)	9265 (2215)	12350 (2950)

Osmolality (mOsm/kg)	2090
pH	5.0 - 6.0

Pharmacotherapeutic group

Solution for parenteral nutrition, combinations
ATC code: B 05BA10

Indications

Supply of energy and essential fatty acids including omega 3 and omega 6 fatty acids, amino acids, electrolytes and fluid in the parenteral nutrition of patients in states of moderate to severe catabolism when oral or enteral nutrition is impossible, insufficient or contraindicated.

Contraindications

This product must not be administered in the presence of the following conditions:
- known hypersensitivity to egg, fish or soy protein, peanut oil or to any of the excipients
- disturbances of amino acid metabolism
- disturbances of lipid metabolism
- hyperkalaemia, hypernatraemia
- 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 without access to haemofiltration or dialysis
- manifest cardiac insufficiency
- aggravating haemorrhagic diatheses
- acute phases of cardiac infarction and stroke
- acute thrombo-embolic events, lipid embolism

On account of its composition Nutriflex Omega special should not be used for neonates, infants and children under 2 years of age.

General contraindications 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.

Special warnings and precautions for use

Caution should be exercised in cases of increased serum osmolarity.

As for all large-volume infusion solutions Nutriflex Omega special should be administered with caution to patients with impaired cardiac or renal function. Disturbances of the fluid, electrolyte or acid-base balance, e.g. hypertonic dehydration, 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 Omega special. Fasting lipaemia should be excluded in patients with suspected disturbances of lipid metabolism before starting infusion.

The administration of lipids is contra-indicated if there is fasting lipaemia. The presence of hypertriglyceridaemia 12 hours after lipid administration also indicates a disturbance of lipid metabolism.

Nutriflex Omega special should be administered cautiously to patients with disturbances of lipid metabolism, e.g. renal insufficiency, diabetes mellitus, pancreatitis, impaired hepatic function, hypothyroidism (with hypertriglyceridaemia), pulmonary disease and sepsis. If Nutriflex Omega special 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 recommended 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.

As with all solutions containing carbohydrates the administration of Nutriflex Omega special 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.

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 product.

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 long-term intravenous nutrition.

Nutriflex Omega special should not be given simultaneously with blood in the same infusion set due to the risk of pseudoagglutination.

Moreover controls of the serum electrolyte levels, 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 Omega special contains zinc and magnesium, care should be taken when it is coadministered with solutions containing these elements.

There is as yet no clinical experience of the use of Nutriflex Omega special in children and adolescents.

There is only limited experience of its use in patients with diabetes mellitus or renal failure.
As with all intravenous solutions strict aseptic precautions are necessary for the infusion of Nutriflex Omega special.

Vitamin E can interfere with the effect of vitamin K in clotting factor synthesis. This should be considered in patients with blood coagulation disorders or suspected vitamin K deficiency.

Nutriflex Omega special is a preparation of complex composition. It is, therefore, strongly advisable not to add other solutions.

Interactions with other medicinal products and other forms of interaction

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 natural 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.

Potassium containing solutions like Nutriflex Omega special should be used with caution in patients receiving drugs that increase serum potassium concentration (e.g. potassium-sparing diuretics, ACE inhibitors, cyclosporine or tacrolimus).

Incompatibilities

Nutriflex Omega special must not be used as a carrier solution for pharmaceuticals or be mixed with other infusion solutions without testing, since it is not possible to guarantee adequate stability of the emulsion.

Pregnancy and lactation

Pregnancy

There is no experience of the use of Nutriflex Omega special in pregnant women. Parenteral nutrition may become necessary during pregnancy. Nutriflex Omega special should only be given to pregnant women after careful consideration.

Lactation

There is no experience of the use of Nutriflex Omega special in nursing mothers. It is as yet not known if Nutriflex Omega special crosses the placental barrier or is excreted in breast milk. No respective data are available from animal experiments either. Breast-feeding is not recommended to mothers on parenteral nutrition.

Dosage

The dosage has to be adapted to the individual requirements of the patient.

It is recommended that Nutriflex Omega special be administered continuously. A stepwise increase of the infusion rate over the first 30 minutes up to the desired infusion rate avoids possible complications.

Adults:

The maximum daily dose amounts to 35 ml per kg body weight, corresponding to
2.0 g amino acids per kg body weight per day
5.04 g glucose per kg body weight per day
1.4 g lipid per kg body weight per day.

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The maximum rate of infusion is 1.7 ml per kg body weight per hour, corresponding to
0.1 g amino acids per kg body weight per hour
0.24 g glucose per kg body weight per hour
0.07 g lipid per kg body weight per hour.

For a patient weighing 70 kg this corresponds to an infusion rate of 119 ml per hour. The amount of amino acid administered is then 6.8 g per hour, of glucose 17.1 g per hour and of lipid per 4.8 g per hour.

In general, it is recommended that the maximum amount of energy should not exceed 40 kcal per kg body weight per day. If specially indicated e.g. for burned patients higher dosage is possible.

Children:

Safety and efficacy in children and adolescents have not been established.

Duration of use

The duration of treatment for the indications stated is not limited. During long-term administration of Nutriflex Omega special it is necessary to provide for appropriate replacement of trace elements and vitamins.

Method of administration

Intravenous use. For central venous infusion only.

Overdose

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 - hyperosmolar coma

Symptoms of lipid overdose

See section 'Undesirable effects'.

Treatment

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

The following listing includes a number of systemic reactions that may be associated with the use of Nutriflex Omega special. Under conditions of correct use, in terms of dosing monitoring, observation of safety restrictions and instructions, most of them are rare (≥ 1/10,000 to < 1/1,000).

Blood and lymphatic system disorders

Very rare (< 1/10,000):	Hypercoagulation

Immune system disorders

Rare (≥ 1/10,000 to < 1/1,000):	Allergic reactions (e.g. anaphylactic reactions, dermal eruptions, laryngeal, oral and facial oedema)

Metabolism and nutrition disorders

Very rare (< 1/10,000):	Hyperlipidaemia, hyperglycaemia, metabolic acidosis, ketoacidosis

The frequency of these undesirable effects is dose-dependent and may be higher under the conditions of absolute or relative lipid overdose.

Nervous system disorders

Rare (≥ 1/10,000 to < 1/1,000):	Drowsiness

Vascular disorders

Rare (≥ 1/10,000 to < 1/1,000):	Hypertension or hypotension, flush

Respiratory, thoracic and mediastinal disorders

Rare (≥ 1/10,000 to < 1/1,000):	Dyspnoea, cyanosis

Gastrointestinal disorders

Uncommon (≥ 1/1,000 to < 1/100):	Nausea, vomiting, loss of appetite

Skin and subcutaneous tissue disorders

Rare (≥ 1/10,000 to < 1/1,000):	Erythema

General disorders and administration site conditions

Rare (≥ 1/10,000 to < 1/1,000):	Headache, elevated body temperature, sweating, feeling cold, chills, pain in the back, bones, chest and lumbar region
Very rare (< 1/10,000):	Fat overload syndrome (details see below)

Should adverse reactions occur or should the triglyceride level rise above 3 mmol/l during infusion, the infusion of Nutriflex Omega special should be stopped or, if necessary, continued at a reduced dosage.

If the infusion is restarted, the patient should be carefully monitored, especially at the beginning, and serum triglycerides should be determined at short intervals.

Triglycerides that contain omega-3 fatty acids may increase bleeding time and inhibit platelet aggregation. In patients with aspirin-induced asthma, pulmonary function may deteriorate as well.

Nausea, vomiting, lack of appetite and hyperglycaemia are symptoms often related to conditions indicating parenteral nutrition or may be associated with parenteral nutrition.

Fat overload syndrome

Impaired capacity to eliminate triglycerides can lead to "Fat overload syndrome" which may be caused by overdose. Possible signs of metabolic overload must be observed. The cause may be genetic (individually different metabolism) or the fat metabolism may be affected by ongoing or previous illnesses. This syndrome may also appear during severe hypertriglyceridaemia, even at the recommended infusion rate, and in association with a sudden change in the patient's clinical condition, such as renal function impairment or infection. The fat overload syndrome is characterised by hyperlipidaemia, fever, fat infiltration, hepatomegaly with or without icterus, splenomegaly, anemia, leukopenia, thrombocytopenia, coagulation disorder, hemolysis and reticulocytosis, abnormal liver function tests and coma. The symptoms are usually reversible if the infusion of the fat emulsion is discontinued.

Should signs of a fat overload syndrome occur, the infusion of Nutriflex Omega special should be discontinued immediately.

Note:

Patients should inform their doctor or pharmacist if they notice any side effect not mentioned in this leaflet.

Expiry date

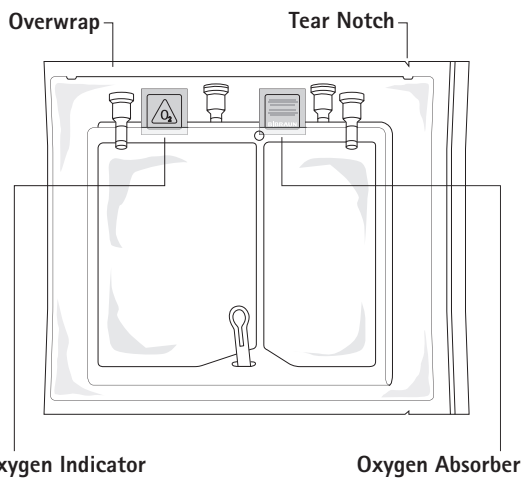
The product must not be used beyond the expiry date stated on the labelling.

Instructions for storage / disposal/ use / handling

Do not store above 25 °C. Do not freeze. If accidentally frozen, discard the bag.

Keep the bags in the outer carton in order to protect from light.

No special requirements are needed for disposal of container, overwrap and oxygen absorber.



The multichamber bag is packed in a protective overwrap. An oxygen absorber and an oxygen indicator are placed between the bag and the overwrap; the oxygen absorber sachet is made of inert material and contains iron hydroxide.

Do not use bags which are damaged. Overwrap, primary bag and the peel seam between the chambers should be intact. Only use if the amino acid and glucose solutions are clear and colourless up to straw coloured and the lipid emulsion is homogenous with milky white appearance. Do not use if the solutions contain particulate matter. After mixing the three chambers, do not use use if the emulsion shows discolouration or signs of phase separation (oil drops, oil layer). Stop the infusion immediately in case of discoloration of the emulsion or signs of phase separation.
Before opening the overwrap, check the colour of the oxygen indicator (see figure). Do not use if the oxygen indicator turned pink. Use only if the oxygen indicator is yellow.

Preparation of the mixed emulsion:

Remove the bag from its protective overwrap and proceed as follows:
- Put the bag on a solid surface
- Open the peel seams of the two upper chambers by pushing with both hands
- Mix the contents of the bag thoroughly.

The mixture is a milky white homogenous oil in water emulsion.

Preparation for infusion:

The emulsion should always be brought to room temperature prior to infusion.
- Fold the bag and hang it on the infusion stand by the centre hanging loop
- Remove the protective cap from the set port and carry out infusion using the standard technique.

If filters are used they must be lipid-permeable.

The emulsion is to be used immediately after opening of the container.

Storage after removing the protective pack and after mixing of the contents of the bag:

Chemical and physical in-use stability after mixing the contents has been demonstrated for 4 days at 2-8°C and 48 hours at 25°C.

Storage after admixture of compatible additives:

From a microbiological point of view, the product 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 admixture has taken place in controlled and validated aseptic conditions.
Nutriflex Omega special is supplied in single dose containers. Unused residues must be discarded.

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