1.3.1.1.1 Approved Professional Information

SCHEDULING STATUS:

S3

1. NAME OF THE MEDICINE

NUTRIFLEX® OMEGA PERI (Emulsion for infusion)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

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

COMPOSITION				
	In 1 000 ml	**In 1 250 ml**	**In 1 875 ml**	**In 2 500 ml**
From the top chamber (glucose solution)				
Glucose monohydrate *(equivalent to anhydrous glucose)*	70,40 g (64,00 g)	88,00 g (80,00 g)	132,0 g (120,0 g)	176,0 g (160,0 g)
Sodium dihydrogen phosphate dihydrate	0,936 g	1,170 g	1,755 g	2,340 g
Zinc acetate dihydrate	5,280 mg	6,600 mg	9,900 mg	13,20 mg
From the middle chamber (fat emulsion)				
Medium chain triglycerides	20,00 g	25,00 g	37,50 g	50,00 g

Soya-bean oil, refined	16,00 g	20,00 g	30,00 g	40,00 g
Omega-3-acid triglycerides	4,000 g	5,000 g	7,500 g	10,00 g
From the bottom chamber (amino acid solution)				
Isoleucine	1,872 g	2,340 g	3,510 g	4,680 g
Leucine	2,504 g	3,130 g	4,695 g	6,260 g
Lysine hydrochloride *(equivalent to lysine)*	2,272 g (1,818 g)	2,840 g (2,273 g)	4,260 g (3,410 g)	5,680 g (4,546 g)
Methionine	1,568 g	1,960 g	2,940 g	3,920 g
Phenylalanine	2,808 g	3,510 g	5,265 g	7,020 g
Threonine	1,456 g	1,820 g	2,730 g	3,640 g
Tryptophan	0,456 g	0,570 g	0,855 g	1,140 g
Valine	2,080 g	2,600 g	3,900 g	5,200 g
Arginine	2,160g	2,700 g	4,050 g	5,400 g
Histidine hydrochloride monohydrate *equivalent to histidine*	1,352 g (1,000 g)	1,690 g (1,251 g)	2,535 g (1,876 g)	3,380 g (2,502 g)
Alanine	3,880 g	4,850 g	7,275 g	9,700 g
Aspartic acid	1,200 g	1,500 g	2,250 g	3,000 g
Glutamic acid	2,800 g	3,500 g	5,250 g	7,000 g

Glycine	1,320 g	1,650 g	2,475 g	3,300 g
Proline	2,720 g	3,400 g	5,100 g	6,800 g
Serine	2,400 g	3,000 g	4,500 g	6,000 g
Sodium hydroxide	0,640 g	0,800 g	1,200 g	1,600 g
Sodium chloride	0,865 g	1,081 g	1,622 g	2,162 g
Sodium acetate trihydrate	0,435 g	0,544 g	0,816 g	1,088 g
Potassium acetate	2,354 g	2,943 g	4,415 g	5,886 g
Magnesium acetate tetrahydrate	0,515 g	0,644 g	0,966 g	1,288 g
Calcium chloride dihydrate	0,353 g	0,441 g	0,662 g	0,882 g
Amino acid content	32 g	40 g	60 g	80 g
Total Nitrogen content	4,6 g	5,7 g	8,6 g	11,4 g
Carbohydrate content	64,0 g	80 g	120 g	160 g
Lipid content	40 g	50 g	75 g	100 g
Electrolyte content (mmol)				
Sodium	40	50	75	100
Potassium	24	30	45	60
Magnesium	2,4	3,0	4,5	6,0
Calcium	2,4	3,0	4,5	6,0
Zinc	0,024	0,03	0,045	0,06

Chloride	38	48	72	96
Acetate	32	40	60	80
Phosphate	6	7,5	11,25	15

	In 1 000 ml	**In 1 250 ml**	**In 1 875 ml**	**In 2 500 ml**
Amino acid content (g)	32	40	60	80
Nitrogen content (g)	4,6	5,7	8,6	11,4
Carbohydrate content (g)	64,0	80	120	160
Lipid content (g)	40	50	75	100

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Emulsion for infusion

Amino acid chamber: Clear, colourless up to faintly straw-coloured solution.

Glucose chamber: Clear, colourless up to faintly straw-coloured solution.

Fat emulsion chamber: A white, milky emulsion.

	In 1000 ml	In 1250 ml	In 1875 ml	In 2500 ml
Energy in the form of lipid [kJ/(kcal)]	1590 (380)	1990 (475)	2985 (715)	3980 (950)
Energy in the form of carbohydrate [kJ/(kcal)]	1075 (255)	1340 (320)	2010 (480)	2680 (640)
Energy in the form of amino acids [kJ/(kcal)]	535 (130)	670 (160)	1005 (240)	1340 (320)
Non-protein energy [kJ/(kcal)]	2665 (635)	3330 (795)	4995 (1195)	6660 (1590)
Total energy [kJ/(kcal)]	3200 (765)	4000 (955)	6000 (1435)	8000 (1910)
Osmolality [mOsm/kg]	950			
Theoretical osmolarity [mOsm/l]	840			
pH	5,0 – 6,0			

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

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

4.2 Posology and method of administration

Posology

The dosage should be adapted to the patients' individual requirements.

It is recommended that **Nutriflex® Omega Peri** be administered as a continuous infusion. 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 is 40 ml/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

The maximum rate of infusion 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 a maximum infusion rate of 175 ml per hour. The amount of substrate administered is then 5,6 g of amino acids per hour, 11,2 g of glucose per hour and 7,0 g of lipids per hour.

Paediatric population

Nutriflex® Omega Peri is contraindicated in newborn infants, infants and toddlers under 2 years of age (see section 4.3).

The safety and efficacy in children over 2 years and adolescents have not been established.

Duration of use

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

Method of administration

For intravenous infusion. Suitable for infusion into a peripheral or central vein.

Refer to section 6.6 for details of handling and preparation.

4.3 Contraindications

Nutriflex® Omega Peri must not be administered in the following conditions:

- Hypersensitivity to the active substances, to egg, fish, peanut or soya protein or to any of the excipients listed in section 6.1
- Disturbances of amino acid metabolism
- Severe hyperlipidaemia characterized by hypertriglyceridaemia (≥ 1000 mg/dL or 11,4 mmol/L)
- Severe coagulopathy
- Hypokalaemia; hyponatraemia
- Unstable metabolism e.g. severe post aggression syndrome (an endocrine imbalance with glucose intolerance and peripheral resistance to insulin, which can result in persistent hyperglycaemic states with increased lipolysis and progressive proteolysis), unstabilised diabetes mellitus 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 in absence of renal replacement therapy

- Manifest cardiac insufficiency
- Aggravating haemorrhagic diatheses
- Acute myocardial infarction and stroke
- Acute event of thromboembolism, lipid embolism

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

General contraindications to parenteral nutrition include:

- Unstable circulatory status

- Inadequate cellular oxygen supply

- Fluid overload/overhydration

- Disturbances of the electrolyte and fluid balance

- Acute pulmonary oedema, decompensated cardiac insufficiency

4.4 Special warnings and precautions for use

Caution should be exercised in cases of increased serum osmolarity.

Disturbances of the fluid, electrolyte or acid-base balance must be corrected before the start of infusion.

Too rapid infusion can lead to fluid overload with pathological serum electrolyte concentrations, hyperhydration and pulmonary oedema.

Any signs or symptoms of anaphylactic reaction (such as fever, shivering, rash or dyspnoea) should lead to immediate interruption of the infusion.

The serum triglyceride concentration should be monitored when infusing **Nutriflex® Omega Peri**.

Depending on the patient's metabolic condition, occasional hypertriglyceridaemia may occur. If the plasma triglyceride concentration rises to more than 4,6 mmol/l (400 mg/dl) during administration

of lipid it is recommended that the infusion rate should be reduced. The infusion must be interrupted if the plasma triglyceride concentration exceeds 11,4 mmol/l (1000 mg/dl), as these levels have been associated with acute pancreatitis.

Patients with impaired lipid metabolism

Nutriflex® Omega Peri should be administered cautiously to patient with disturbances of lipid metabolism with increased serum triglycerides, e.g. renal insufficiency, diabetes mellitus, pancreatitis, impaired hepatic function, hypothyroidism (with hypertriglyceridaemia), sepsis and metabolic syndrome. If **Nutriflex® Omega Peri** is given to patients with these conditions, more frequent monitoring of serum triglycerides is necessary to assure triglyceride elimination and stable triglyceride levels below 11,4 mmol/l (1000 mg/dl).
In combined hyperlipidaemias and in metabolic syndrome, triglyceride levels react to glucose, lipids and overnutrition. Adjust dose accordingly. Assess and monitor other lipid and glucose sources, and medicines interfering with their metabolism.
The presence of hypertriglyceridaemia 12 hours after lipid administration also indicates a disturbance of lipid metabolism.

The administration of **Nutriflex® Omega 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. If the patient is receiving other intravenous glucose solutions concurrently, the amount of additionally administered glucose has to be taken into account.

An 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.

Refeeding, commencing or recommencing nutrition therapy in malnourished or depleted patients may cause hypokalaemia, hypophosphataemia and hypomagnesaemia. Close monitoring of serum electrolytes is mandatory. Adequate supplementation of electrolytes according to deviations from normal values is necessary.

Controls of the serum electrolytes, the water balance, acid-base balance, and of blood cell counts, coagulation status, renal and hepatic function are necessary.

Substitution of electrolytes, vitamins and trace elements may be necessary as required. As **Nutriflex® Omega Peri** contains zinc, magnesium, calcium and phosphate, care should be taken when it is co-administered with solutions containing these elements.

Nutriflex® Omega Peri is a preparation of complex composition. It is, therefore, strongly advisable not to add other solutions (as long as compatibility is not proven – see section 6.2).
Additions can increase the overall osmolarity of the emulsion, consider with regard to peripheral administration and monitor the injection site.

Nutriflex® Omega Peri should not be given simultaneously with blood in the same infusion set due to the risk of pseudoagglutination (see also section 4.5).

As with all intravenous solutions, especially for parenteral nutrition, strict aseptic precautions are necessary for the infusion of **Nutriflex® Omega Peri**.

Infusion in peripheral veins may cause thrombophlebitis. Monitor infusion site daily for signs of thrombophlebitis.

Paediatric population

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

Elderly patients

Basically, the same dosage as for adults applies, but caution should be exercised in patients suffering from further diseases like cardiac insufficiency or renal insufficiency that may frequently be associated with advanced age.

Patients with diabetes mellitus, impaired cardiac or renal function

Like all large-volume infusion solutions, **Nutriflex® Omega Peri** should be administered with caution to patients with impaired cardiac or renal function.

There is only limited experience of its use in patients with diabetes mellitus or renal failure.

Nutriflex® Omega Peri *contains sodium*

This medicine contains 1150 mg sodium per 1250 ml bag, equivalent to 58 % of the WHO recommended maximum daily intake of 2 g sodium for an adult.

The maximum daily dose of this product for a 70 kg adult is equivalent to 129 % of the WHO recommended maximum daily intake for sodium.

Nutriflex® Omega Peri is considered high in sodium. This should be particularly taken into account for those on a low salt diet.

Interference with laboratory tests:

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.

4.5 Interaction with other medicinal products and other forms of interaction

Some medicines, 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 medicines.

Potassium-containing solutions like **Nutriflex® Omega Peri** should be used with caution in patients receiving medicines that increase serum potassium concentration, such as potassium-sparing diuretics (triamterene, amiloride, spironolactone), ACE inhibitors (e.g. captopril, enalapril), angiotensin-II-receptor antagonists (e.g. losartan, valsartan), ciclosporin and tacrolimus.

Corticosteroids and ACTH are associated with sodium and fluid retention.

Nutriflex® Omega Peri should not be given simultaneously with blood products in the same infusion set due to the risk of pseudoagglutination (see also section 4.4).

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no or limited amount of data from the use of **Nutriflex® Omega Peri** in pregnant women. Animal studies are insufficient with respect to reproductive toxicity (see section 5.3). Parenteral nutrition may become necessary during pregnancy. Nutriflex Omega Plus should only be given to pregnant women after careful consideration.

Lactation

Components/metabolites of **Nutriflex® Omega Peri** are excreted in human milk, but at therapeutic doses no effects on the breastfed newborn/infants are anticipated. Nevertheless, breast-feeding is not recommended for mothers on parenteral nutrition.

Fertility

No data from the use of **Nutriflex® Omega Peri** is available.

4.7 Effects on ability to drive and use machines

Nutriflex® Omega Peri has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Under conditions of correct use, adherence to dosage and observation of safety restrictions and instructions, undesirable effects may still occur. The following listing includes a number of systemic reactions that may be associated with the use of **Nutriflex® Omega Peri**.

<u>Blood and lymphatic system disorders:</u>

Less frequent: Hypercoagulation.

Frequency unknown: Leukopaenia, thrombocytopenia, hypokalaemia, hypophosphataemia, hypomagnesaemia.

Immune system disorders:

Less frequent: Allergic reactions (e.g. anaphylactic reactions, dermal eruptions, laryngeal, oral and facial oedema).

Metabolism and nutrition disorders:

Less frequent: Loss of appetite, hyperlipidaemia, hyperglycaemia, metabolic acidosis.

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

Nervous system disorders:

Less frequent: Headache, drowsiness.

Vascular disorders:

Less frequent: Hypertension or hypotension, flush.

Respiratory, thoracic and mediastinal disorders:

Less frequent: Dyspnoea, cyanosis.

Gastrointestinal disorders:

Less frequent: Nausea, vomiting.

Hepatobiliary disorders:

Frequency unknown: Cholestasis.

Skin and subcutaneous tissue disorders:

Less frequent: Erythema, sweating

Musculoskeletal and connective tissue disorders:

Less frequent: Back ache, pain in the chest, bones and lumbar region.

General disorders and administration site conditions:

Frequent: After a few days, vein irritation, phlebitis or thrombophlebitis may occur.

Less frequent: Elevated body temperature, feeling cold, chills, Fat overload syndrome (see below for details).

If signs of vein wall irritation, phlebitis, or thrombophlebitis occur, change of the infusion site should be considered.

Should adverse reactions occur, the infusion must be stopped.

Should the triglyceride level rise to above 11,4 mmol/l (1000 mg/dl) during infusion, the infusion must be stopped. With levels above 4,6 mmol/l (400 mg/dl), the infusion may be continued at a reduced dosage (see section 4.4).

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

Information on particular undesirable effects

Nausea, vomiting and lack of appetite are symptoms often related to conditions for which parenteral nutrition is indicated and may be associated with parenteral nutrition at the same time.

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, anaemia, leucopenia, thrombocytopenia, coagulation disorder, haemolysis 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 Peri** should be discontinued immediately.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

4.9 Overdose

Symptoms of fluid and electrolyte overdose

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, glycosuria, dehydration, hyperosmolality, hyperglycaemic-hyperosmolar coma.

Symptoms of lipid 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 if platelet count, reduction in white cell count, haemorrhagic diathesis and haemorrhage, alternation of depression of blood coagulation factors (bleeding time, coagulation time, prothrombin time, etc.).(See section 4.8.).

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.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacological classification: A.24. Mineral substitutes, electrolytes and trace elements

Pharmacotherapeutic group: Solutions for parenteral nutrition, combinations

ATC code: B 05BA10

Mechanism of action

The purpose of parenteral nutrition is to supply all necessary nutrients and energy for the growth and/or regeneration of tissue as well as for the maintenance of all body functions.

Amino acids are of particular importance since some of them are essential components for protein synthesis. The simultaneous administration of energy sources (carbohydrates/lipids) is necessary to reserve amino acids for tissue regeneration and anabolism and prevent their utilisation as energy source.

Glucose is ubiquitously metabolised within the organism. Some tissues and organs, such as CNS, bone marrow, erythrocytes, tubular epithelium, cover their energy requirement exclusively from glucose. In addition glucose acts as a structural building block for various cell substances.

On account of their high energy density, lipids are an efficient form of energy supply. Long-chain triglycerides provide the organism with essential fatty acids for the synthesis of cell components. For this purpose the fat emulsion contains medium-chain and long-chain triglycerides (deriving from soya-bean oil).

The long-chain triglyceride fraction contains omega-6 and omega-3 triglycerides for supply of polyunsaturated fatty acids. They are primarily intended for the prevention and treatment of essential fatty acid deficiency, but also as a source of energy. **Nutriflex® Omega Peri** contains essential omega-6 fatty acids, mainly in the form of linoleic acid, and omega-3 fatty acids in the form of alpha- linolenic acid, eicosapentaenoic acid, and docosahexaenoic acid. The ratio of omega-6 to omega-3 fatty acids in **Nutriflex® Omega Peri** is approximately 2,5:1.

Medium-chain triglycerides are more rapidly hydrolysed, eliminated from the circulation and completely oxidised than long-chain triglycerides. They are a favoured energy substrate, particularly when there is disturbance of the degradation and/or utilisation of long-chain triglycerides, e.g. when there is a lipoprotein lipase deficiency and/or a deficiency in lipoprotein lipase cofactors.

5.2 Pharmacokinetic properties

Absorption

Nutriflex® Omega Peri is infused intravenously. Hence, all substrates are available for metabolism immediately.

Distribution

The dose, rate of infusion, metabolic situation and individual factors of the patient (level of fasting) are of decisive importance for the maximum triglyceride concentrations reached. When used according to the instructions with due regard to the dosage guidelines the triglyceride concentrations do not, in general, exceed 4,6 mmol/l (400 mg/dl).

Medium-chain fatty acids have a low affinity to albumin. In animal experiments administering pure medium-chain triglyceride emulsions, it has been shown that medium-chain fatty acids can cross the blood-brain barrier, if overdosed. No adverse effects were observed with an emulsion providing a mixture of medium-chain triglycerides and long-chain triglycerides, as long-chain triglycerides have an inhibiting effect on medium-chain triglyceride hydrolysis. Therefore, toxic effects on the brain can be excluded after the administration of **Nutriflex® Omega Peri**.

Amino acids are incorporated in a variety of proteins in different organs of the body. In addition, each amino acid is maintained as free amino acid in the blood and inside cells.

As glucose is water-soluble, it is distributed with the blood over the whole body. At first, the glucose solution is distributed in the intravascular space and then it is taken up into the intracellular space.

No data are available concerning transport of the components through the placental barrier.

Biotransformation

Amino acids that do not enter protein synthesis are metabolised as follows. The amino group is separated from the carbon skeleton by transamination. The carbon chain is either oxidised directly to CO_2 or utilised as substrate for gluconeogenesis in the liver. The amino group is also metabolised in the liver to urea.

Glucose is metabolised to CO_2 and H_2O via the known metabolic routes. Some glucose is utilised for lipid synthesis.

After infusion, triglycerides are hydrolysed to glycerol and fatty acids. Both are incorporated in physiological pathways for energy production, synthesis of biological active molecules, gluconeogenesis and resynthesis of lipids.

In detail, long-chain omega-3 polyunsaturated fatty acids replace arachidonic acid as an eicosanoid substrate in cell membranes and decrease the generation of inflammatory eicosanoids and cytokines in the body. This may be of benefit in patients at risk of developing a hyperinflammatory state and sepsis.

Elimination

Only minor amounts of amino acids are excreted unchanged in urine.

Excess glucose is excreted in urine only if the renal threshold of glucose is reached.

Both the triglycerides of soya-bean oil and medium-chain triglycerides are completely metabolised to CO_2 and H_2O. Small amounts of lipids are lost only during sloughing of cells from skin and other epithelial membranes. Renal excretion does virtually not occur.

5.3 Preclinical safety data

Preclinical studies, including safety pharmacology, reproductive and developmental toxicity studies, with a lipid emulsion containing twice the amount of omega-3 acid triglycerides and a correspondingly smaller amount of omega-6 triglycerides revealed no effects other than those expected following administration of high doses of lipids.

Toxic effects of mixtures of nutrients given as substitution therapy at the recommended dosage are not to be expected.

Reproductive toxicity

Phytoestrogens such as ß-sitosterol can be found in various vegetable oils, especially in soya-bean oil. Impairment of fertility was determined in rats and rabbits after subcutaneous and intravaginal administration of ß-sitosterol. After administration of pure ß-sitosterol a decrease of the testicular weight and a reduction of the sperm concentration in male rats and a lowered pregnancy rate in female rabbits were recorded. However, according to the current state of knowledge the observed effects in animals do not seem to have relevance for clinical use.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Citric acid monohydrate (for pH adjustment)

Glycerol

Egg phospholipids for injection

Sodium oleate

All-rac-α-Tocopherol

Sodium hydroxide (for pH adjustment)

Water for injections

6.2 Incompatibilities

Nutriflex® Omega Peri must not be mixed with other medicines for which compatibility has not been documented. See section 6.6.

Nutriflex® Omega Peri should not be given simultaneously with blood, see sections 4.4 and 4.5.

6.3 Shelf life

Unopened

2 years

After removing the protective overwrap and after mixing of contents of the bag

Chemical and physicochemical in-use stability of the mixture of amino acids, glucose and fat was demonstrated for 7 days at 2 to 8 °C and additional 2 days at 25 °C.

After admixture of compatible additives

From a microbiological point of view, the product should be used immediately after admixture of additives. If not used immediately after admixture of additives, in-use storage times and conditions prior to use are the responsibility of the user.

After first opening (penetration of the infusion port)

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

6.4 Special precautions for storage

Protect from light and store at or below 25 °C.

Do not freeze. If accidentally frozen, discard the bag.

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

KEEP OUT OF REACH OF CHILDREN.

6.5 Nature and contents of container

Nutriflex® Omega Peri is supplied in flexible multi-chamber bags of multi-layer foil. The inner layer in contact with the solution consists of polypropylene. The twin-base port is made of polypropylene and styrene ethylene butylene styrene. The multi-chamber bags contain:

- 1250 ml (500 ml of amino acids solution + 250 ml of fat emulsion + 500 ml of glucose solution)
- 1875 ml (750 ml of amino acids solution + 375 ml of fat emulsion + 750 ml of glucose solution)
- 2500 ml (1000 ml of amino acids solution + 500 ml of fat emulsion + 1000 ml of glucose solution).

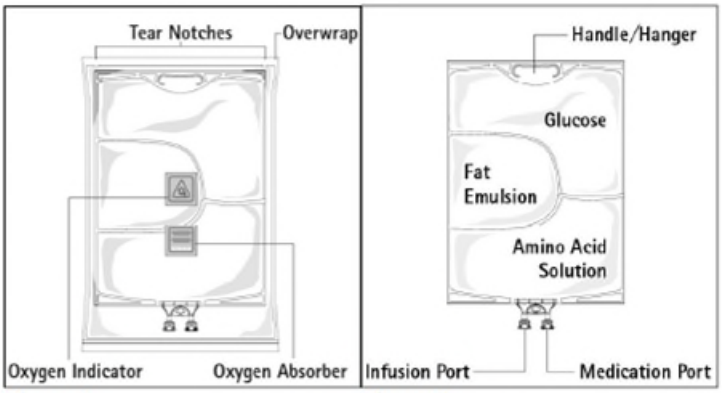

Figure A Figure B

Figure A: The multi-chamber 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.

Figure B: The top chamber contains a glucose solution, the middle chamber contains a fat emulsion, and the bottom chamber contains an amino acid solution.

The top chamber and the middle chamber can be connected with the bottom chamber by opening the intermediate seams (peel seams).

The design of the bag permits mixing of the amino acids, glucose, lipids and electrolytes in a single chamber. Opening the peel seams results in sterile mixing to form an emulsion.

The different container sizes are presented in cartons containing five bags.
Pack sizes: 5 x 1250 ml; 5 x 1875 ml; 5 x 2500 ml.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements for disposal.
Parenteral nutrition products should be visually inspected for damage, discolouration and emulsion instability before use.

Do not use bags which are damaged. Overwrap, primary bag and the peel seams between the chambers should be intact. Only use if the amino acid and glucose solutions are clear and colourless up to faintly 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 if the emulsion shows discolouration or signs of phase separation (oil drops, oil layer). Stop the infusion immediately in case of discolouration of the emulsion or signs of phase separation.

Before opening the overwrap, check the colour of the oxygen indicator (see Figure A). Do not use if the oxygen indicator turned pink. Use only if the oxygen indicator is yellow.

Preparation of mixed emulsion

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 center hanging loop.

• Remove the protective cap from the run-out port and carry out infusion using the normal technique.

7. HOLDER OF CERTIFICATE OF REGISTRATION

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8. APPLICATION/REGISRATION NUMBER:

57/24/0881

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

21 July 2026

10. DATE OF REVISION OF THE TEXT

N/A