B BRAUN

## Professional Information

**SCHEDULING STATUS:**

S3

**1. NAME OF THE MEDICINE**

**NUTRIFLEX® LIPID PLUS** (Intravenous infusion)

**2. QUALITATIVE AND QUANTITATIVE COMPOSITION**

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

| **COMPOSITION:** | | | |
|---|---|---|---|
| | **In 1250 mL** | **In 1875 mL** | **In 2500 mL** |
| **From upper, left-hand chamber (glucose solution)** | | | |
| Glucose monohydrate<br>*equivalent to glucose* | 165,0 g<br>150,0 g | 247,50 g<br>225,0 g | 330,0 g<br>300,0 g |
| Sodium dihydrogen phosphate dihydrate | 2,34 g | 3,51 g | 4,68 g |
| Zinc acetate dihydrate | 6,58 mg | 9,87 mg | 13,16 mg |
| **From upper, right-hand chamber (fat emulsion)** | | | |
| Medium-chain triglycerides | 25,0 g | 37,5 g | 50,0 g |
| Soybean oil refined | 25,0 g | 37,5 g | 50,0 g |
| **From lower chamber (amino acid solution)** | | | |
| Isoleucine | 2,82 g | 4,23 g | 5,64 g |
| Leucine | 3,76 g | 5,64 g | 7,52 g |
| Lysine hydrochloride<br>*equivalent to lysine* | 3,41 g<br>2,73 g | 5,12 g<br>4,10 g | 6,82 g<br>5,46 g |

| | | | |
|---|---|---|---|
| Methionine | 2,35 g | 3,53 g | 4,70 g |
| Phenylalanine | 4,21 g | 6,32 g | 8,42 g |
| Threonine | 2,18 g | 3,27 g | 4,36 g |
| Tryptophan | 0,68 g | 1,02 g | 1,36 g |
| Valine | 3,12 g | 4,68 g | 6,24 g |
| Arginine | 3,24 g | 4,86 g | 6,48 g |
| Histidine hydrochloride monohydrate<br>*equivalent to histidine* | 2,03 g<br>1,50 g | 3,05 g<br>2,25 g | 4,06 g<br>3,00 g |
| Alanine | 5,82 g | 8,73 g | 11,64 g |
| Aspartic acid | 1,80 g | 2,70 g | 3,60 g |
| Glutamic acid | 4,21 g | 6,32 g | 8,42 g |
| Glycine | 1,98 g | 2,97 g | 3,96 g |
| Proline | 4,08 g | 6,12 g | 8,16 g |
| Serine | 3,60 g | 5,40 g | 7,20 g |
| Sodium hydroxide | 0,976 g | 1,464 g | 1,952 g |
| Sodium chloride | 0,503 g | 0,755 g | 1,006 g |
| Sodium acetate trihydrate | 0,277 g | 0,416 g | 0,554 g |
| Potassium acetate | 3,434 g | 5,151 g | 6,868 g |
| Magnesium acetate tetrahydrate | 0,858 g | 1,287 g | 1,716 g |
| Calcium chloride dihydrate | 0,588 g | 0,882 g | 1,176 g |
| Amino acid content | 48,0 g | 72,0 g | 96,0 g |
| Nitrogen content | 6,8 g | 10,2 g | 13,6 g |
| Carbohydrate content | 150,0 g | 225,0 g | 300,0 g |
| Lipid content | 50,0 g | 75,0 g | 100,0 g |
| **Electrolytes (mmol)** | In 1250 mL | In 1875 mL | In 2500 mL |
| Sodium | 50,0 | 75,0 | 100,0 |

| | | | |
|---|---|---|---|
| Potassium | 35,0 | 52,5 | 70,0 |
| Magnesium | 4,0 | 6,0 | 8,0 |
| Calcium | 4,0 | 6,0 | 8,0 |
| Zinc | 0,03 | 0,045 | 0,06 |
| Chloride | 45,0 | 67,5 | 90,0 |
| Acetate | 45,0 | 67,5 | 90,0 |
| Phosphate | 15,0 | 22,5 | 30,0 |

For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Intravenous 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 oil-in-water emulsion.

| | In 1250 mL | In 1875 mL | In 2500 mL |
|---|---|---|---|
| Energy in the form of lipid [kJ/(kcal)] | 1990 (475) | 2985 (715) | 3980 (950) |
| Energy in the form of carbohydrate [kJ/(kcal)] | 2510 (600) | 3765 (900) | 5020 (1200) |
| Energy in the form of amino acids [kJ/(kcal)] | 800 (190) | 1200 (285) | 1600 (380) |
| Non-protein energy [kJ/(kcal)] | 4500 (1075) | 6750 (1615) | 9000 (2155) |
| Total energy [kJ/(kcal)] | 5300 (1265) | 7950 (1900) | 10600 (2530) |
| Osmolality [mOsm/kg] | 1540 | 1540 | 1540 |
| Theoretical osmolarity [mOsm/L] | 1215 | 1215 | 1215 |
| pH | 5,0 – 6,0 | 5,0 – 6,0 | 5,0 – 6,0 |

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic 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.

### 4.2 Posology and method of administration

**Posology**

The dosage is adjusted according to the patient's individual requirements.

The maximum daily dose is 40 mL /kg body weight, corresponding to:

- 1,54 g amino acids /kg body weight per day
- 4,8 g glucose /kg body weight per day
- 1,6 g fat /kg body weight per day

It is recommended that **Nutriflex® Lipid Plus** be administered continuously. A stepwise increase of the infusion rate over the first 30 minutes up to the desired infusion rate helps to avoid complications.

The maximum rate of infusion is 2,0 mL/kg body weight per hour, corresponding to

- 0,08 g amino acids /kg body weight per hour
- 0,24 g glucose /kg body weight per hour
- 0,08 g fat /kg body weight per hour

For a patient weighing 70 kg this corresponds to an infusion rate of 140 mL per hour. The amount of amino acid administered is then 5,4 g/hour, of glucose 16,8 g/hour and of lipid 5,6 g/hour.

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

**Method of administration**

The ready-to-use emulsion is infused into a central vein.

The emulsion should always be brought to room temperature prior to infusion.

Only intact containers, with homogenous fat emulsions after gentle shaking, and clear solutions, are to be used.

**Duration of use**

The duration of treatment for the indications stated in not limited. During long-term administration of **Nutriflex® Lipid Plus** it is necessary to supply appropriate replacement of trace elements and vitamins.

**4.3 Contraindications**

- Hypersensitivity to the active substances, to egg, peanut or soya protein or to any of the excipients listed in section 6.1
- Disturbances of amino acid metabolism
- Disturbances of lipid metabolism
- 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
- Manifest cardiac insufficiency

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

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

General contraindications to parenteral nutrition include:

- Unstable circulatory status
- Acute phases of cardiac infarction and stroke
- Unstable metabolic condition (e.g. severe postaggression syndrome, coma of unknown origin)
- Inadequate cellular oxygen supply
- 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, e.g. hyperhydration, hyperkalaemia, acidosis, 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 sign of 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® Lipid Plus**.

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.

*Patients with impaired lipid metabolism*

**Nutriflex® Lipid Plus** should be administered cautiously to patients with disturbances of lipid metabolism, e.g. renal insufficiency, diabetes mellitus, pancreatitis, impaired liver function, hypothyroidism, sepsis and metabolic syndrome. If **Nutriflex® Lipid Plus** is given to patients with these conditions close monitoring of serum triglycerides is mandatory.

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 normalises.

The administration of **Nutriflex® Lipid Plus** 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.

A dose reduction or interruption of administration of the emulsion may be indicated if the blood glucose concentration rises to above 14 mmol/L (250 mg/dL) during administration.

Refeeding or repletion of malnourished or depleted patients may cause hypokalaemia, hypophosphataemia and hypomagnesaemia. Adequate supplementation of electrolytes according to deviations from normal values is necessary.

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.

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® Lipid Plus** contains zinc, magnesium, calcium and phosphate, care should be taken when it is co-administered with solutions containing these substances.

**Nutriflex® Lipid Plus** should not be given simultaneously with blood in the same infusion set due to the risk of pseudoagglutination.

**Nutriflex® Lipid Plus** 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).

As with all intravenous solutions strict aseptic precautions are necessary for the infusion of **Nutriflex® Lipid Plus**.

*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 or renal function*

Like all large-volume infusion solutions, **Nutriflex® Lipid Plus** should be administered with caution to patients with impaired renal function.

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

***Nutriflex® Lipid Plus** contains sodium*

**Nutriflex® Lipid Plus** 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 **Nutriflex® Lipid Plus** for a 70 kg adult is equivalent to 129 % of the WHO recommended maximum daily intake for sodium. **Nutriflex® Lipid Plus** 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 medication, 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 agents.

Potassium-containing solutions like **Nutriflex® Lipid Plus** should be used with caution in patients receiving drugs 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® Lipid Plus** should not be given simultaneously with blood in the same infusion set due to the risk of pseudoagglutination (see also section 4.4).

Solutions containing amino acids, carbohydrate and lipids should not be mixed with other solutions due to the risk for incompatibilities or microbial contamination. Concomitant infusion with other medicines should also be avoided due to the risk of incompatibilities (see section 6.2).

**4.6 Fertility, pregnancy and lactation**

Pregnancy

Safety and efficacy have not yet been established. **Nutriflex® Lipid Plus** is manufactured with soybean oil that contains phytosterols in concentrations that could lead to disturbances of fertility.

Lactation

Breastfeeding is not recommended if women need parenteral nutrition.

Fertility

No data from the use of **Nutriflex Lipid Plus** available.

**4.7 Effects on ability to drive and use machines**

**Nutriflex® Lipid Plus** has no or negligible influence on the ability to drive and use machines.

**4.8 Undesirable effects**

Under conditions of correct use, in terms of dosing monitoring, 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® Lipid Plus**.

Blood and lymphatic system disorders:

*Less frequent:* Hypercoagulation.

*Frequency unknown:* Hypokalaemia, hypophosphataemia, hypomagnesaemia, hypermagnesaemia, leucopenia, thrombocytopenia.

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.

*Frequency unknown:* Respiratory distress.

Gastrointestinal disorders:

*Less frequent:* Nausea, vomiting.

Hepatobiliary disorders:

*Frequency unknown:* Cholestasis.

Skin and subcutaneous tissue disorders:

*Less frequent:* Erythema, sweating

*Frequency unknown:* Bluish discoloration of the skin due to reduced oxygen content of the blood (cyanosis).

Musculoskeletal and connective tissue disorders:

*Less frequent:* Pain in the back, bones, chest and lumbar region.

Cardiac disorders:

*Frequency unknown:* Fall or increase in blood pressure.

General disorders and administration site conditions:

*Frequent:* Thrombophlebitis.

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

*Frequency unknown:* Infection of the injection site which can lead to septicaemia; irritation at the injection site.

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® Lipid Plus** 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 ‘6.04 Adverse Drug Reactions Reporting Form’. Found under SAHPRA’s publications:

https://www/sahpra.org.za/Publications/Index/8

**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:*

Refer to section 4.8.

*Treatment*

Immediate cessation of infusion is indicated in the case of 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. 25 Special Foods

Pharmacotherapeutic group: Solutions for parenteral nutrition, combinations

ATC code: B05BA10

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.

*Lipids*

The lipid component of **Nutriflex® Lipid Plus** contains equal quantities of soybean oil (long-chain triglycerides, LCT) and medium-chain triglycerides (MCT). Soybean oil consists of more than 50% of the polyunsaturated fatty acids linoleic acid and α-linolenic acid. MCT are included as a high calorie source.

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 these purposes the fat emulsion contains medium-chain and long-chain triglycerides (deriving from soya-bean oil).

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.

Unsaturated fatty acids derived from the long-chain triglyceride fraction serve primarily for prophylaxis and treatment of essential fatty acid deficiency.

*Carbohydrates*

In order to ensure optimal utilization of the amino acids delivered with the nutrient solution, and to improve the emulsion triglyceride utilization, an energy source is required. This can be partly fulfilled by carbohydrates namely glucose monohydrate.

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.

*Amino acids*

**Nutriflex® Lipid Plus** contains all essential amino acids and the non-essential amino acids.

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.

*Electrolytes*

**Nutriflex® Lipid Plus** contains all the essential electrolytes, i.e. sodium, potassium, magnesium, calcium and phosphate. It also contains the trace element zinc.

**5.2 Pharmacokinetic properties**

Absorption

**Nutriflex® Lipid Plus** 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® Lipid Plus**.

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.

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**

Non-clinical studies have not been performed with **Nutriflex® Lipid Plus**. 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. 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 lecithin

Sodium oleate

Water for injections

### 6.2 Incompatibilities

**Nutriflex® Lipid Plus** must not be mixed with other medicinal products for which compatibility has not been documented. See section 6.6.

**Nutriflex® Lipid Plus** 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 4 days at 2 - 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 (spiking of the infusion port)*

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

**6.4 Special precautions for storage**

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

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

The emulsion is to be used immediately after mixing. It can be stored for 7 days at 2-8 °C and for 48 hours at 25 °C.

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

**6.5 Nature and contents of container**

**Nutriflex® Lipid Plus** is manufactured as a transparent colourless three chamber bag. The two upper compartments of this bag are connected with the lower compartment by peel seams. The bag is made of a co-extruded film of Polyamide 11 and Polypropylene (V90 film) packed in a carton.

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**

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 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.

*Preparation of mixed solution*

Remove the inner bag from its protective pack and proceed as follows:

- Open out the bag and lay on a solid surface.
- Mix glucose with amino acids by pressing the upper left chamber against the peel seam, then add the fat emulsion by pressing the upper right chamber against the peel seam.
- 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 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.

For single use only.

Container and unused residues must be discarded after use.

Do not reconnect partially used containers.

If filters are used they must be lipid-permeable (pore size ≥ 1,2 µm).

**7. HOLDER OF CERTIFICATE OF REGISTRATION**

B Braun Medical (Pty) Ltd

253 Aintree Road,

North Riding

Gauteng

South Africa 2194

Tel: +27 (010) 222 3000

Fax: +27 (010) 222 3133

**8. REGISTRATION NUMBER:**

41/25/0756

**9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

11 February 2011

**10. DATE OF REVISION OF THE TEXT**

16 May 2023