## SUMMARY OF PRODUCT CHARACTERISTICS

### 1. NAME OF THE MEDICINAL PRODUCT

NuTRIflex® Lipid plus Emulsion for Infusion

### 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Nutriflex Lipid plus Emulsion for Infusion contains:

<table>
<thead>
<tr>
<th>Chamber Description</th>
<th>Size 1</th>
<th>Size 2</th>
<th>Size 3</th>
<th>Quantity per 1000 ml</th>
</tr>
</thead>
</table>
| **Glucose monohydrate,**
  equivalent to anhydrous glucose | 165.0 g | 247.5 g | 330.0 g | 132.0 g |
| **Sodium dihydrogen phosphate dihydrat** | 2.340 g | 3.510 g | 4.680 g | 1.870 g |
| **Zinc acetate dihydrat** | 6.58 mg | 9.87 mg | 13.16 mg | 5.25 mg |

<table>
<thead>
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<th>Size 2</th>
<th>Size 3</th>
<th>Quantity per 1000 ml</th>
</tr>
</thead>
</table>
| **Soya bean oil,**
  refined | 25.0 g | 37.5 g | 50.0 g | 20.0 g |
| **Medium-chain triglycerides** | 25.0 g | 37.5 g | 50.0 g | 20.0 g |

<table>
<thead>
<tr>
<th>Chamber Description</th>
<th>Size 1</th>
<th>Size 2</th>
<th>Size 3</th>
<th>Quantity per 1000 ml</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Isoleucine</strong></td>
<td>2.82 g</td>
<td>4.23 g</td>
<td>5.64 g</td>
<td>2.26 g</td>
</tr>
<tr>
<td><strong>Leucine</strong></td>
<td>3.76 g</td>
<td>5.64 g</td>
<td>7.52 g</td>
<td>3.01 g</td>
</tr>
</tbody>
</table>
| **Lysine hydrochloride,**
  equivalent to Lysine | 3.41 g | 5.12 g | 6.82 g | 2.73 g |
| **Methionine** | 2.35 g | 3.52 g | 4.70 g | 1.88 g |
| **Phenylalanine** | 4.21 g | 6.31 g | 8.42 g | 3.37 g |
| **Threonine** | 2.18 g | 3.27 g | 4.36 g | 1.74 g |
| **Tryptophan** | 0.68 g | 1.02 g | 1.36 g | 0.54 g |
| **Valine** | 3.12 g | 4.68 g | 6.24 g | 2.50 g |
| **Arginine** | 3.24 g | 4.86 g | 6.48 g | 2.50 g |
| **Histidine hydrochloride monohydrate,**
  equivalent to Histidine | 2.03 g | 3.05 g | 4.06 g | 1.62 g |
| **Alanine** | 5.82 g | 8.73 g | 11.64 g | 4.66 g |
| **Aspartic acid** | 1.80 g | 2.70 g | 3.60 g | 1.44 g |
| **Glutamic acid** | 4.21 g | 6.32 g | 8.42 g | 3.37 g |
| **Glycine** | 1.98 g | 2.97 g | 3.96 g | 1.58 g |
| **Proline** | 4.08 g | 6.12 g | 8.16 g | 3.26 g |
| **Serine** | 3.60 g | 5.40 g | 7.20 g | 2.88 g |
from the lower chamber (500, 750 and 1000 ml)

<table>
<thead>
<tr>
<th></th>
<th>in 1250 ml Size 1</th>
<th>in 1875 ml Size 2</th>
<th>in 2500 ml Size 3</th>
<th>Quantity per 1000 ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium chloride dihydrate</td>
<td>0.588 g</td>
<td>0.882 g</td>
<td>1.176 g</td>
<td>0.470 g</td>
</tr>
<tr>
<td>Magnesium acetate tetrahydrate</td>
<td>0.858 g</td>
<td>1.286 g</td>
<td>1.716 g</td>
<td>0.686 g</td>
</tr>
<tr>
<td>Sodium acetate trihydrate</td>
<td>0.277 g</td>
<td>0.416 g</td>
<td>0.554 g</td>
<td>0.222 g</td>
</tr>
<tr>
<td>Sodium chloride</td>
<td>0.503 g</td>
<td>0.755 g</td>
<td>1.006 g</td>
<td>0.402 g</td>
</tr>
<tr>
<td>Potassium acetate</td>
<td>3.434 g</td>
<td>5.151 g</td>
<td>6.868 g</td>
<td>2.747 g</td>
</tr>
<tr>
<td>Sodium hydroxide</td>
<td>0.976 g</td>
<td>1.464 g</td>
<td>1.952 g</td>
<td>0.781 g</td>
</tr>
</tbody>
</table>

Electrolytes [mmol]

<table>
<thead>
<tr>
<th></th>
<th>in 1250 ml Size 1</th>
<th>in 1875 ml Size 2</th>
<th>in 2500 ml Size 3</th>
<th>Quantity per 1000 ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>50</td>
<td>75</td>
<td>100</td>
<td>40</td>
</tr>
<tr>
<td>Potassium</td>
<td>35</td>
<td>52.5</td>
<td>70</td>
<td>28</td>
</tr>
<tr>
<td>Magnesium</td>
<td>4.0</td>
<td>6.0</td>
<td>8.0</td>
<td>3.2</td>
</tr>
<tr>
<td>Calcium</td>
<td>4.0</td>
<td>6.0</td>
<td>8.0</td>
<td>3.2</td>
</tr>
<tr>
<td>Chloride</td>
<td>45</td>
<td>67.5</td>
<td>90</td>
<td>36</td>
</tr>
<tr>
<td>Acetate</td>
<td>45</td>
<td>67.5</td>
<td>90</td>
<td>36</td>
</tr>
<tr>
<td>Phosphate</td>
<td>15</td>
<td>22.5</td>
<td>30</td>
<td>12</td>
</tr>
<tr>
<td>Zinc</td>
<td>0.03</td>
<td>0.04</td>
<td>0.06</td>
<td>0.024</td>
</tr>
</tbody>
</table>

Aminoacid content (g)

<table>
<thead>
<tr>
<th></th>
<th>in 1250 ml Size 1</th>
<th>in 1875 ml Size 2</th>
<th>in 2500 ml Size 3</th>
<th>Quantity per 1000 ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aminoacid content</td>
<td>48</td>
<td>72</td>
<td>96</td>
<td>38</td>
</tr>
<tr>
<td>Nitrogen content</td>
<td>6.8</td>
<td>10.2</td>
<td>13.6</td>
<td>5.4</td>
</tr>
<tr>
<td>Carbohydrate content</td>
<td>150</td>
<td>225</td>
<td>300</td>
<td>120</td>
</tr>
<tr>
<td>Lipid content</td>
<td>50</td>
<td>75</td>
<td>100</td>
<td>40</td>
</tr>
</tbody>
</table>

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Emulsion for infusion.

The lower chamber and the larger upper chamber (amino acids and glucose solutions): clear, colourless up to faintly straw-coloured solutions.

The smaller top chamber (lipid emulsion): oil-in-water emulsion, milky white.

Physico-chemical characteristics of Nutriflex Lipid plus after mixing the chamber contents:
4. CLINICAL PARTICULARS

4.1 Therapeutic indications
Supply of energy, essential fatty acids, amino acids, electrolytes and fluids in the setting of parenteral nutrition of patients in states of moderately severe catabolism when oral or enteral nutrition is impossible, insufficient or contraindicated.

4.2 Posology and method of administration

Posology
The dosage is adapted to the patients’ individual requirements.

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 avoids possible complications.

Adolescents from 14 years of age and adults
The maximum daily dose amounts to 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 lipid /kg body weight per day.

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 lipid /kg body weight per hour.

For a patient weighing 70 kg this corresponds to a maximum infusion rate of 140 ml per hour.
The amount of substrate administered is then 5.4 g of amino acids per hour, 16.8 g of glucose per hour and 5.6 g of lipids per hour.

Paediatric population

Newborn infants, infants and toddlers less than two years of age
Nutriflex Lipid plus is contraindicated in newborn infants, infants and toddlers < 2 years of age (see section 4.3).

**Children from 2 to 13 years of age**
The given dosage recommendations are guiding data based on average requirements. The dosage should be individually adapted according to age, developmental stage and illness. For calculation of dosage account must be taken of the hydration status of the paediatric patient.

For children, it might be necessary to start the nutritional therapy with half of the target dosage. The dosage should be increased stepwise according to the individual metabolic capacity up the maximum dosage.

**Daily dose for 2 – 4 years of age:**
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 lipid/kg body weight per day.

**Daily dose for 5 – 13 years of age:**
25 ml/kg body weight, corresponding to:
- 0.96 g amino acids/kg body weight per day
- 3.0 g glucose/kg body weight per day
- 1.0 g lipid/kg body weight per day.

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 lipid/kg body weight per hour.

Due to the individual needs of paediatric patients, NuTRIflex® Lipid plus may not cover sufficiently the total energy and fluid requirements. In such cases carbohydrates and/or lipids and/or fluids must be provided in addition, as appropriate.

**Patients with renal/hepatic impairment**
The doses should be adjusted individually in patients with hepatic or renal insufficiency (see also section 4.4).

**Duration of treatment**
The duration of treatment for the indications stated is not limited. During long-term administration of NuTRIflex® Lipid plus it is necessary to provide for appropriate supply of trace elements and vitamins.

**Method of administration**
Intravenous use. For central venous infusion only.

### 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
- congenital disorders of amino acid metabolism
- severe hyperlipidaemia
- 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
• aggravating haemorrhagic diatheses
• acute thrombo-embolic events, lipid embolism

On account of its composition, NuTRIflex® Lipid plus must not be used in newborn infants, infants and toddlers under 2 years of age.

General contraindications to parenteral nutrition include:
• unstable circulatory status with vital threat (states of collapse and shock)
• 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 case of increased serum osmolarity.

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

Any sign or symptom 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. Depending on the patient’s metabolic condition, occasional hypertriglyceridaemia may occur. If the plasma triglyceride concentration rises to above 3 mmol/l during administration of lipids it is recommended that the infusion rate be reduced. Should the plasma triglyceride concentration remain above 3 mmol/l, the administration should be stopped until the level normalises.

Like all solutions containing carbohydrates, administration of NuTRIflex® Lipid plus can lead to hyperglycaemia. The blood glucose levels 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 of the emulsion may be indicated if the blood glucose concentration rises to above 14 mmol/l (250 mg/dl) during administration.

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.

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

**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 Lipid plus 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.

**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 hepatic function, hypothyroidism (with hypertriglyceridaemia) and sepsis. If NuTRIflex® Lipid plus is given to patients with these conditions, monitoring of serum triglycerides is necessary. The presence of hypertriglyceridaemia 12 hours after lipid administration also indicates a disturbance of lipid metabolism.

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

Controls of the serum electrolytes, the water balance, the acid-base balance, and – during long-term administration – of blood cell counts, coagulation status and hepatic function are necessary.

Substitution of electrolytes, vitamins and trace elements may be necessary as required.

As NuTRIflex® Lipid plus contains zinc and magnesium, care should be taken when it is co-administered with solutions containing these elements.

As with all intravenous solutions, strict aseptic precautions are necessary for the infusion of NuTRIflex® Lipid plus.

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).

**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 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 K₁. 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® 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), cyclosporin and tacrolimus.

Corticosteroids and ACTH are associated with sodium and fluid retention.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no or limited amount of data from the use of NuTRIflex® Lipid plus in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).

Parenteral nutrition may become necessary during pregnancy. NuTRIflex® Lipid plus should only be given to pregnant women after careful consideration.

Breast-feeding

Components/metabolites of NuTRIflex® Lipid plus are excreted in human milk, but at therapeutic doses no effects on the breastfed newborns/infants are anticipated. Nevertheless, breast-feeding is not recommended for mothers on parenteral nutrition.

Fertility

No data available.

4.7 Effects on ability to drive and use machines

Not relevant

4.8 Undesirable effects

The following listing includes a number of systemic reactions that may be associated with the use of NuTRIflex® Lipid plus. 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).

Undesirable effects are listed according to their frequencies as follows:

- Very common: (≥ 1/10)
- Common: (≥ 1/100 to < 1/10)
- Uncommon: (≥ 1/1,000 to < 1/100)
- Rare: (≥ 1/10,000 to < 1/1,000)
- Very rare: (< 1/10,000)
- Not known: (frequency cannot be estimated from the available data)

Blood and lymphatic system disorders

Rare: Hypercoagulation

Immune system disorders

Rare: Allergic reactions (e.g. anaphylactic reactions, dermal eruptions, laryngeal, oral and facial oedema)
**Metabolism and nutrition disorders**

Very rare: Hyperlipidaemia, hyperglycaemia, metabolic acidosis, ketoacidosis
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**

Rare: Drowsiness

**Vascular disorders**

Rare: Hypertension or hypotension, flush

**Respiratory, thoracic and mediastinal disorders**

Rare: Dyspnoea, cyanosis

**Gastrointestinal disorders**

Uncommon: Nausea, vomiting, loss of appetite

**Skin and subcutaneous tissue disorders**

Rare: Erythema

**General disorders and administration site conditions**

Rare: Headache, elevated body temperature, sweating, feeling cold, chills, pain in the back, bones, chest and lumbar region

Very rare: Fat overload syndrome (details see below)

Should adverse reactions occur or should the triglyceride level rise to above 3 mmol/l during infusion, the infusion 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.

**Information on particular undesirable effects**

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, anaemia, leukopenia, 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 side effects**

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at: [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard).

By reporting side effects you can help provide more information on the safety of this medicine.
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, glucosuria, dehydration, hyperosmolality, hyperglycaemic-hyperosmolar coma.

*Symptoms of lipid overdose*
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

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 for the growth and regeneration of tissue as well as energy necessary to maintain all body functions.

Here the 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 avoid false energetic utilisation of amino acids while still providing for the further energy-consuming processes.

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 these purposes the lipid 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.

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 3 mmol/l.

When the dosage guidelines are followed, medium-chain fatty acids and long-chain fatty acids are practically completely bound to plasma albumin. Therefore, when the dosage guidelines are followed, medium and long-chain fatty acids do not pass the blood-brain barrier and, hence, do not pass into the cerebrospinal fluid.

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 CO₂ or utilised as substrate for gluconeogenesis in the liver. The amino group is also metabolised in the liver to urea.

Glucose is metabolised to CO₂ and H₂O 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 CO₂ and H₂O. 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 data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential.

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

**Reproductive toxicity**
Phytoestrogens such as β-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 β-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)
- Egg lecithin
- Glycerol
- Sodium oleate
- Water for injections

6.2 **Incompatibilities**
In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 **Shelf life**

*Unopened:*
2 years

*After removing the protective overwrap and after mixing of contents of the bag*
Chemical and physical in-use stability after mixing the contents has been demonstrated for 7 days at 2-8 °C plus 48 hours at 25 °C.

*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**
- Do not store above 25 °C.
- Do not freeze.
- Keep the bag in the outer carton in order to protect from light.

6.5 **Nature and contents of container**
NuTRIflex® Lipid plus is supplied in flexible multichamber bags of polyamide/polypropylene containing:

- 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)

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

The two upper chambers can be connected with the lower chamber by opening the intermediate seam (peel seam).

The design of the bag permits mixing of the amino acids, glucose, lipids and electrolytes in a single chamber. Opening the peel seam 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 and 5 x 2500 ml

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and handling

Preparation of the mixed emulsion:
Remove inner bag from its protective overwrap and proceed as follows:
- put the bag on a solid, flat 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.

Preparation for infusion:
- fold the bag and hang it on the infusion stand by the centre hanging loop
- remove the protective cap from the infusion port and carry out infusion using the standard technique

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

Only use bags that are undamaged and in which the amino acid and glucose solutions are clear and colourless up to faintly straw-coloured solutions. Do not use bags where there is a discolouration or discernible phase separation (oil drops) in the chamber containing lipid emulsion.

NuTRIflex® Lipid plus is supplied in single dose containers. Container and unused residues must be discarded after use.

Do not reconnect partially used containers.

The emulsion should always be brought to room temperature prior to infusion.
If accidentally frozen discard the bag.

If filters are used they must be lipid-permeable.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements

7 MARKETING AUTHORISATION HOLDER

B. Braun Melsungen AG
Carl Braun Str. 1
34212 Melsungen
Germany

8 Marketing Authorisation Number

PL 03551/0029

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORIZATION

Date of first authorization: 12/05/1998
Date of latest renewal: 25/02/2009

10 DATE OF REVISION OF THE TEXT

04/08/2014