SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Lipofundin MCT/LCT 20 %, emulsion for infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1000 ml emulsion for infusion contain:	
Soya-bean oil, refined	100.0 g
Medium-chain triglycerides (MCT)	100.0 g
Essential fatty acid content per 1000 ml:	
Linoleic acid	48.0 – 58.0 g
α-Linolenic acid	5.0 – 11.0 g

Excipient(s) with known effect

Lipofundin MCT/LCT 20% contains less than 1 mmol (23 mg) sodium per litre.
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Emulsion for infusion
Milky-white oil-in-water emulsion

Energy [kJ/l (kcal/l)]	8095 (1935)
Theoretical osmolarity [mOsm/l]	380
Acidity or alkalinity (titration to pH 7.4) [mmol/l]	< 0.5
pH	6.0 - 8.5

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Lipofundin MCT/LCT is indicated as a source of calories and essential fatty acids for patients requiring parenteral nutrition.

4.2 Posology and method of administration

Posology

Maximum daily doses should only be administered after stepwise increase with careful monitoring of the tolerance of the infusions.
The utilisation of intravenous lipids depends on e.g. the severity of underlying disease, body weight, gestational and postnatal age and specific body functions.
Depending on energy requirements, the following daily doses are recommended:

Adults

The usual dose is **0.7 to 1.5 g** lipids/kg body weight (b.w.) per day. A maximum dose of **2.0 g** lipids/kg b.w./d, for instance when energy requirements are high or fat utilisation is increased (e.g. oncology patients), should not be exceeded. For long-term home parenteral nutrition treatment (> 6 months) and in patients with short bowel syndrome the provision of intravenous lipids should not exceed **1.0 g/kg b.w./d**.
For a patient weighing 70 kg a daily dose of 2.0 g/kg b.w./d corresponds to a maximum daily dose of 700 ml Lipofundin MCT/LCT 20%.

Paediatric population

A gradual increase of lipid intake in increments of 0.5 – 1.0 g/kg b.w./d may be beneficial regarding the possibility to monitor the increase of the plasma triglyceride level and prevent hyperlipidaemia.

Preterm newborn infants, term newborn infants, infants and toddlers
It is recommended not to exceed a daily dose of **3.0 (max. 4.0) g/kg b.w./d** of lipids.
In preterm newborn infants, term newborn infants, infants and toddlers, the daily dose of lipids should be infused continuously over about 24 hours.

Children and adolescents
It is recommended not to exceed a daily lipid dose of **2.0** – **3.0 g/kg b.w./d**.

Infusion rate

The infusion should be administered at the lowest possible infusion rate. During the first 15 minutes the infusion rate should only be 50% of the maximum infusion rate to be used.
The patient should be monitored closely for the occurrence of adverse reactions.

Maximum infusion rate

Adults
Up to **0.15 g/kg b.w./h** lipids.
For a patient weighing 70 kg this corresponds to a maximum infusion rate of 52.5 ml per hour Lipofundin MCT/LCT 20%. The amount of lipids administered then is 10.5 g per hour.

Preterm newborn infants, term newborn infants, infants and toddlers
Up to **0.17 g/kg b.w./h** lipids.

Children and adolescents
Up to **0.13 g/kg b.w./h** lipids.

Method of administration

Intravenous use.

Lipid emulsions are suitable for peripheral venous administration and can also be administered separately via peripheral veins as part of total parenteral nutrition.

The Y- or the bypass connector should be placed as close to the patient as possible, if lipid emulsions are co-administered with amino acid and carbohydrate solutions.

The duration of administration of Lipofundin MCT/LCT 20% is usually 1 - 2 weeks. If parenteral nutrition with lipid emulsions is further indicated, Lipofundin MCT/LCT 20% can be administered over longer periods provided appropriate monitoring is employed.

When used in infants aged from preterm to 2 years old, the emulsion (including administration sets) should be protected from light exposure after preparation for infusion until administration is completed (see sections 4.4, 6.3 and 6.6).

4.3 Contraindications

- Hypersensitivity to egg or soya-bean protein, soya-bean or peanut products or to any of the active substances or the excipients listed in section 6.1.
- Severe hyperlipidaemia
- Severe coagulopathy
- Severe hepatic insufficiency
- Intrahepatic cholestasis
- Severe renal insufficiency in absence of renal replacement therapy
- Acute thromboembolic events
- Fat embolism
- Aggravating haemorrhagic diatheses
- Metabolic acidosis

General contraindications to parenteral nutrition include:
- Unstable circulatory status with vital threat (states of collapse and shock)
- Unstable metabolic conditions (e.g. severe post-aggression syndrome, severe sepsis, coma of un-known origin)
- Acute phase of myocardial infarction or stroke
- Uncorrected disorders of fluid and electrolyte balance, such as hypokalaemia and hypotonic dehy-dration (see also section 4.4)
- Decompensated cardiac insufficiency
- Acute pulmonary oedema

4.4 Special warnings and precautions for use

The serum triglyceride concentration should be regularly monitored during the infusion of Lipofundin MCT/LCT 20%.

Depending on the patient’s metabolic condition, occasional hypertriglyceridaemia may occur. If the plasma triglyceride concentration exceeds 4.6 mmol/l during administration of the lipid emulsion, it is recommended to reduce the infusion rate. The infusion must be interrupted if the plasma triglyceride concentration exceeds 11.4 mmol/l.

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

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

Hypersensitivity reactions to an ingredient of Lipofundin MCT/LCT 20% (e.g. due to traces of protein in soya-bean oil or egg phospholipids for injection) are extremely rare, but cannot be totally excluded for sensitised patients. Infusion of Lipofundin MCT/LCT should immediately be discontinued in case of appearance of any sign of allergic reaction, e.g. fever, shivering, rash, dyspnoea.

Energy supply with lipid emulsions alone could cause metabolic acidosis. It is therefore recommended to infuse an adequate quantity of intravenous carbohydrates and amino acids along with the fat emulsion.

For patients requiring complete parenteral nutrition, complementary carbohydrate, amino acid, electrolyte, vitamin, and trace element supplements are required. Also, an adequate total fluid intake has to be ensured.

Mixing with incompatible substances might lead to breaking of the emulsion or to precipitation of particles (see sections 6.2 and 6.6), both resulting in a high risk of embolism.

In solutions with higher lipid concentration (e.g. Lipofundin MCT/LCT 20%), the ratio of emulsifier (phospholipid) to oil is lower than in lower concentrated lipid emulsions. This ensures a favourable lower plasma concentration of triglycerides, phospholipids, free fatty acids as well as the pathological lipoprotein-X in the patient`s blood. Therefore higher concentrated lipid emulsions like Lipofundin MCT/LCT 20% should be preferred over lower concentrated lipid emulsions.

Elderly patients

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 impaired lipid metabolism

Lipofundin MCT/LCT 20% 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 Lipofundin MCT/LCT 20% is administered to patients with these conditions, close monitoring of serum triglycerides is necessary. The dose should be adjusted to the metabolic tolerance. The presence of hypertriglyceridaemia 12 hours after lipid administration also indicates a disturbance of lipid metabolism.

Paediatric population

Free fatty acids (FFA) compete with bilirubin for albumin binding sites. Especially very premature infants may be at increased risk of hyperbilirubinaemia due to high levels of FFA released from triglycerides resulting in a high FFA/albumin ratio. In parenterally fed infants at risk of hyperbilirubinaemia, serum triglyceride and bilirubin levels should be monitored and lipid infusion rate be adjusted if deemed necessary. During infusion Lipofundin MCT/LCT 20% should be protected from phototherapy light to decrease the formation of potentially harmful triglyceride hydroperoxides.

The serum triglyceride concentration should be regularly monitored during the infusion of Lipofundin MCT/LCT 20%, especially if there is an increased risk of hyperlipidaemia. A stepwise increase of the daily dose may be advisable.
Depending on the patient's metabolic condition, occasional hypertriglyceridaemia may occur. In infants dose reduction should be considered if the plasma triglyceride concentration during infusion exceeds 2.8 mmol/l. In older children dose reduction should be considered if the plasma triglyceride concentration during infusion exceeds 4.5 mmol/l.

Light exposure of mixtures for intravenous parenteral nutrition, especially after admixture with trace elements and/or vitamins, may have adverse effects on clinical outcome in neonates, due to generation of peroxides and other degradation products. When used in infants aged from preterm to 2 years old, Lipofundin MCT/LCT 20% should be protected from light exposure after preparation for infusion until administration is completed (see sections 4.2, 6.3 and 6.6).

Interference with laboratory tests

Lipids may interfere with certain laboratory tests (such as bilirubin, lactate dehydrogenase, oxygen saturation) when the blood sample is taken before the lipids have been eliminated from the bloodstream; this may take 4 to 6 hours.

4.5 Interaction with other medicinal products and other forms of interaction

- **Heparin**

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.

- **Coumarin derivatives**

Soya-bean oil has a natural content of vitamin K1. The content is however so low in Lipofundin MCT/LCT 20% that it is not expected to influence the coagulation process significantly in patients treated with coumarin derivatives. Nevertheless, the coagulation status should be monitored in patients treated concomitantly with coumarins.

4.6 Fertility, pregnancy and lactation

Pregnancy
There are no or limited amount of data from the use of Lipofundin MCT/LCT 20% in pregnant women. Animal data are insufficient with respect to reproductive toxicity (see section 5.3).
Parenteral nutrition may become necessary during pregnancy. Lipofundin MCT/LCT 20% should only be administered to pregnant women after careful benefit-risk consideration.

Breastfeeding

Components / metabolites of Lipofundin MCT/LCT 20% are excreted in human milk, but at therapeutic doses no effects on the breastfed newborns / infants are anticipated. In general, breastfeeding is not recommended to mothers receiving parenteral nutrition.

Fertility
No human data available. Animal studies have indicated no evidence of an effect on fertility.

4.7. Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

The following listing includes a number of systemic adverse reactions that may be associated with the use of Lipofundin MCT/LCT 20%. Under the conditions of correct use, in terms of dosing, monitoring, observation of safety restrictions and instructions, most of them are very rare (< 1/10,000).

Listing of undesirable effects

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
Very rare: Hypercoagulability
Not known: Leucopenia, thrombocytopenia

Immune system disorders
Very 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 adverse reactions is dose-dependent and may be higher under conditions of absolute or relative overdose.

Nervous system disorders
Very rare: Headache, drowsiness

Vascular disorders

Very rare: Hypertension or hypotension, flush

Respiratory, thoracic and mediastinal disorders
Very rare: Dyspnoea, cyanosis

Gastrointestinal disorders
Very rare: Nausea, vomiting, loss of appetite

Hepatobiliary disorders
Not known: Cholestasis

Skin and subcutaneous tissue disorders
Very rare: Erythema, sweating

Musculoskeletal and connective tissue disorders
Very rare: Pain in the back, bones, chest and lumbar region

General disorders and administration site conditions
Very rare: Elevated body temperature, feeling cold, chills, fat overload syndrome (see below).

If adverse reactions occur, the infusion of Lipofundin MCT/LCT 20% must be stopped or, if necessary, continued at a reduced dosage.

If the infusion is restarted, the patient must 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 related to conditions constituting an indication for parenteral nutrition and may sometimes be associated with parenteral nutrition.

Fat overload syndrome
Overdose of lipid emulsion or impaired capacity to eliminate triglycerides can lead to "fat overload syn-drome". 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 diseases.
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 Lipofundin MCT/LCT 20% must be discon-tinued 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 via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Symptoms
Hyperlipidaemia, metabolic acidosis.
Also, a fat overload syndrome may occur. See section 4.8.

Treatment
Immediate cessation of infusion is indicated for overdose. Other therapeutic measures will depend on the particular symptoms and their severity.
When the infusion is recommenced after 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

Lipofundin MT/LCT 20% provides a source of energy and essential (polyunsaturated) fatty acids for the patient requiring parenteral nutrition. Medium-chain triglycerides are cleared from the bloodstream at a faster rate and are oxidised more completely for energy production than long-chain triglycerides. For that reason they serve as preferential fuel for the body, especially in conditions where the oxidation of long-chain triglycerides is impaired, eg due to carnitine deficiency or diminished carnitine palmitoyl-transferase activity, resp.

The polyunsaturated fatty acids, which are only provided by long-chain triglycerides, will prevent the biochemical disorders of essential fatty acid deficiency (EFAD), and correct the clinical manifestations of the EFAD syndrome.

Pharmacotherapeutic group:	Solutions for parenteral nutrition, fat emulsions
ATC code:	B05B A02

5.2. Pharmacokinetic properties

Because of the I.V administration of Lipofundin MCT/LCT 20%, no data on absorption are provided; for the same reason, the bio-availability is 100 per cent.

The maximum serum triglyceride concentrations during infusion of Lipofundin MCT/LCT mainly depend on the actual dose and infusion rate as well as on the patient's individual metabolic status and other patient-related factors, e.g. the fasting triglyceride level. In general, however, serum

triglyceride concentrations will not exceed 5 µmol/l as long as recommended doses and all other directions for use are observed.

The plasma half-life time of triglycerides infused in the form of Lipofundin MCT/LCT 20% is approx 9 minutes. Although the affinity of long-chain fatty acids to albumin is somewhat greater than that of medium-chain fatty acids, albumin binding of both types of fatty acids is virtually complete, provided the recommended doses are not exceeded. Therefore, medium- and long-chain fatty acids do not pass over the cerebrospinal fluid. No data are presently available as to passage across the placental barrier and into breastmilk.

Triglycerides and free fatty acids are not excreted via the kidneys. In view of the intended nutritive effects of Lipofundin MCT/LCT 20% , such excretion is not even desirable. Poisoning requiring rapid elimination of the toxic agent is not to be expected with Lipofundin MCT/LCT 20% because this product only contains physiological nutrient substances.

5.3. Preclinical safety data

The pharmacological and toxicological studies conducted with the product did not reveal any effects indicating specific pharmacological activity or toxicity of the product relevant to its use in man at the recommended dose levels.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glycerol: 25.0 g/l
Egg phospholipids for injection: 12.0 g/l
all-rac-α-Tocopherol: 170 mg/l
Sodium oleate (for pH-adjustment)
Water for injections

6.2 Incompatibilities

Lipofundin MCT/LCT 20 % must not be used as carrier solutions for electrolyte concentrates or other pharmaceuticals nor must the emulsion be mixed with other infusion solutions, since adequate stability of the emulsion would no longer be guaranteed.

Combined regimens are only to be used for parenteral nutrition after their pharmaceutical compatibility has been controlled and guaranteed.

The combination of Lipofundin MCT/LCT 20 % with alcohol-containing infusion or injection solutions must be avoided.

6.3 Shelf life

Unopened
2 years

After first opening the container
After first opening the medicinal product should be used immediately.
When used in infants aged from preterm to 2 years old, the emulsion (including administration sets) should be protected from light exposure after preparation for infusion until administration is completed (see sections 4.2, 4.4 and 6.6).

After reconstitution or dilution
Not applicable, see section 6.2.

6.4 Special precautions for storage

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

6.5 Nature and contents of container

- Glass bottles (type II glass) sealed with rubber stoppers:

Contents: 100 ml, available in packs of 10 x 100 ml
250 ml, available in packs of 10 x 250 ml
500 ml, available in packs of 10 x 500 ml

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements for disposal.

If filters are used, these must be permeable to lipids.

Before infusing a lipid emulsion together with other solutions via a Y connector or bypass set, the compatibility of these fluids should be checked, especially when co-administering carrier

solutions to which drugs have been added. Particular caution should be exercised when co-infusing solutions that contain divalent electrolytes (such as calcium or magnesium).

Shake gently prior to use.

The emulsion has to be brought to room temperature unaided prior to infusion, i.e., the product should not be put in a heating device (such as oven or microwave).

For single use only. Any unused emulsion should be discarded.

Products that have been frozen should be discarded.

Only use containers that are undamaged and in which the emulsion is homogenous and milky white. Inspect the emulsion visually for phase separation prior to administration.

When used in infants aged from preterm to 2 years old, parenteral nutrition mixtures containing Lipofundin MCT/LCT should be protected from light exposure, after preparation for infusion until administration is completed. Exposure of such mixtures to light, especially after admixture with trace elements and/ or vitamins, generates peroxides and other degradation products that can be reduced by protection from light exposure (see sections 4.2, 4.4 and 6.3).

7 MARKETING AUTHORISATION HOLDER

B. Braun Melsungen AG
Carl-Braun-Straße 1
34212 Melsungen

Postal address:
34209 Melsungen
Germany

Telephone: +49-5661-71-0
Fax: +49-5661-71-4567

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