Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Lipofundin MCT/LCT 10 % w/v Emulsion for Infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1000ml emulsion contains :
Active ingredients :

Soya-Bean Oil	50.0	g
Medium-chain Triglycerides	50.0	g

For excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Emulsion for infusion
A white, milky oil-in-water emulsion.

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. Where such nutrition is required for extended periods of time (more than 5 days), it is also indicated as a source of essential fatty acids to prevent the clinical manifestations of Essential Fatty Acid Deficiency (EFAD).

4.2 Posology and method of administration

1. Adults and school-age children

1-2 g fat per kg body weight per day, corresponding to 10-20 ml of Lipofundin MCT/LCT 10 % per kg body weight per day.

2. Neonates, infants and pre-school children

Neonates

2-3 g (up to 4 g) of fat per kg body weight per day, corresponding to 20-30 ml (up to 40 ml) of Lipofundin MCT/LCT 10 % per kg body weight per day.

Especially in preterm infants and low-birth-weight neonates, the ability to eliminate infused lipids is not yet fully developed. Therefore maximum fat doses (3-4 g per kg body weight) should not be administered to these patients and serum triglyceride and fatty acid levels should be carefully monitored.

At the end of the daily fat-free interval, the fat must have been cleared from the serum.

Infants and pre-school children

1-3 g of fat per kg body weight per day, corresponding to 10-30 ml of Lipofundin MCT/LCT 10 % per kg body weight per day.

3. The elderly

There is no evidence to suggest that dosage should be different from that recommended for other adult patients. Nevertheless, metabolic rates and patterns can vary in the elderly, so careful monitoring of this particular group of patients is always prudent.

Infusion rates

In general, fat emulsions should be infused at as low a rate as possible. During the first 15 minutes the infusion rate should not exceed 0.05 - 0.1 g of fat per kg body weight per hour, corresponding to 0.5 - 1.0 ml Lipofundin MCT/LCT 10 % per kg body weight per hour. If no adverse reactions are observed during this initial phase, the infusion rate may be increased to 0.15 - 0.2 g fat per kg body weight per hour, corresponding to 1.5 - 2.0 ml of Lipofundin MCT/LCT 10 % per kg body weight per hour. The daily fat infusions should be administered over not less than 16 hours, preferably as continuous infusion over 24 hours.

Duration of use

In total parenteral nutrition, Lipofundin MCT/LCT is normally administered over 1-2 weeks (up to 4 weeks max.). In elective cases, if fat infusions are further indicated and appropriate monitoring is instituted, the period of use of Lipofundin MCT/LCT may be extended beyond 4 weeks.

Lipofundin MCT/LCT should be administered as part of a total parenteral nutrition regimen via peripheral vein or central venous catheter.

Lipofundin MCT/LCT can be infused into the same central or peripheral vein as the carbohydrate and amino acid solutions by means of a short Y-connector near the infusion site. This allows for mixing of the solutions immediately before entering the vein. Flow rates of each solution should be controlled separately by infusion pumps, if these are used.

Fat emulsions should be allowed to warm up to room temperature before infusion.

For safe administration of intravenous fluids from non-collapsible containers a giving set with an integral airway is recommended.

Infusion sets with in-line filters of less than 5 micrometers (µm) porosity are not to be used for administration of fat emulsions.

4.3 Contraindications

The administration of Lipofundin MCT/LCT is contra-indicated in patients demonstrating disturbances in normal fat metabolism such as pathologic hyperlipaemia, lipoid nephrosis, or acute pancreatitis if accompanied by hyperlipaemia. It is further contra-indicated in patients with ketoacidosis or hypoxia, in thromboembolism and in acute shock states.

4.4 Special warnings and precautions for use

Caution should be exercised in administering intravenous fat emulsions in patients with metabolic acidosis, severe liver damage, pulmonary disease, sepsis, diseases of the reticuloendothelial system, anaemia or blood coagulation disorders or when there is danger of fat embolism.

The too rapid infusion of fat emulsions can cause fluid and/or fat overloading resulting in dilution of serum electrolyte concentrations, overhydration, congested states, pulmonary oedema, impaired pulmonary diffusion capacity.

A too rapid infusion of Lipofundin MCT/LCT can also cause hyperketonaemia and/or metabolic acidosis, especially when carbohydrates are not administered simultaneously.

Administration of Lipofundin MCT/LCT should be accompanied by simultaneous carbohydrate infusions making up to 40 % (at least) of the total calorie intake and should be administered as part of a total parenteral nutrition regime.

When Lipofundin MCT/LCT is administered, the patient's capacity to eliminate the infused fat from the circulation must be monitored. The lipaemia must clear between daily infusions. Especially where fat emulsions are administered for extended periods of time, the patient's haemogram, blood coagulation, liver function and platelet count should be

closely monitored.

4.5 Interaction with other medicinal products and other forms of interaction

None known;
for Incompatibilities, however, see section 6.2.

4.6 Pregnancy and lactation

The safety of Lipofundin MCT/LCT during pregnancy and lactation has not been definitely assessed. It is not known whether Lipofundin MCT/LCT can cause foetal harm when administered to a pregnant woman or can affect reproduction capacity.

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

Adverse reactions directly related to fat emulsions in general are of two types:

(a) Immediate (acute) reactions: dyspnea, cyanosis, allergic reactions, hyperlipaemia, hypercoagulability, nausea, vomiting, headache, flushing, hyperthermia, sweating, chills, sleepiness, chest and back pain.

(b) Delayed reactions: hepatomegaly, jaundice due to central lobular cholestasis, splenomegaly, thrombocytopenia, transient increases in liver function tests, and overloading syndrome. The deposition of a brown pigmentation in the reticuloendothelial system, the so-called "intravenous fat pigment", has also been reported. The cause and the significance of this phenomenon are unknown.

4.9 Overdose

In the event of fat overload during therapy, stop the infusion of Lipofundin MCT/LCT, until visual inspection of the plasma, determination of triglyceride concentrations, or measurement of plasma light-scattering activity by nephelometry indicate the lipid has cleared. Re-evaluate the patient and institute appropriate corrective measures.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Lipofundin MCT/LCT 10 % 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, e.g. due to carnitine deficiency or diminished carnitine palmitoyltransferase 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.

Phosphatides as contained in egg lecithin are involved in the formation of membrane structures and warrant their fluidity and biological functions.

Glycerol is metabolised in the body as an energy donor or is used in the synthesis of body glycogen and fat.

5.2 Pharmacokinetic properties

Because of the i. v. administration of Lipofundin MCT/LCT 10 %, no data on absorption are to be provided; for the same reason, the bio-availability is 100 per cent.

The maximum serum triglyceride concentrations during infusion of Lipofundin MCT/LCT 10 % 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 micromol/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 10 % 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 into the cerebrospinal fluid. No data are presently available as to passage across the placental barrier and into breast milk.
Triglycerides and free fatty acids are not excreted via the kidneys. In view of the intended nutritive effect of Lipofundin MCT/LCT 10 %, such excretion is not even desirable. Poisoning requiring rapid elimination of the toxic agent is not to be expected with Lipofundin MCT/LCT 10 % 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
Egg lecithin
Sodium oleate
Alpha tocopherol
Water for injections

6.2 Incompatibilities

As a general rule fat emulsions should not be mixed with electrolytes, drugs or any other additives in the infusion bottle.

Lipofundin MCT/LCT 10% may be used with nutrient mixing bag systems only if such resultant mixtures are compatible and stable.

6.3 Shelf Life

Unopened: 2 years.

6.4 Special precautions for storage

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

6.5 Nature and contents of container

Lipofundin MCT/LCT 10% is supplied in glass bottles, sealed with rubber stoppers.
Contents: 100ml, 250ml, 500ml.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

Lipofundin MCT/LCT 10% is supplied in single dose containers. Unused contents must be discarded and should not be stored for later use.

Infusion sets with in-line filters of less than 5 micrometers (μm) porosity should not be used for administration of fat emulsions.

Do not use any bottle in which there appears to be a separation (oiling out) of the emulsion or if bottle is damaged.

7 MARKETING AUTHORISATION HOLDER

B Braun Medical Limited
3 Naas Road Industrial Park
Dublin 12

8 MARKETING AUTHORISATION NUMBER

PA 179/31/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 23 January 1991

Date of last renewal: 23 January 2006

10 DATE OF REVISION OF THE TEXT

February 2006