

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 contains:

Soya-bean oil	100.0 g
Medium-chain triglycerides (MCT)	100.0 g

Essential fatty acid content:

Linoleic acid	48.0 - 58.0 g/l
α -Linolenic acid	5.0 - 11.0 g/l

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

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

Energy	7990 kJ/l \square 1908 kcal/l
Theoretical osmolarity	380 mOsm/l
Acidity or alkalinity, titration to pH 7.4	< 0.5 mmol/l

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

1. Adults and school-age children

1-2 g fat per kg body weight per day, corresponding to 5-10 ml of lipofundin MCT/LCT 20% 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 10-15 ml (up to 20 ml) of Lipofundin MCT/LCT 20% 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 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 5-15 ml of Lipofundin MCT/LCT 20% 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 0.25-0.5 ml of Lipofundin MCT/LCT 20% 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 0.75-1.0 ml of Lipofundin MCT/LCT 20% per kg per hour. The daily fat infusions should be administered over not less than 15 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.

Method of Administration

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 infusions 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:

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 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

Special Warnings

Dependence, tolerance: not applicable.

Other

The too rapid infusion of fat emulsions can cause fluid and/or 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.

Vitamin E can interfere with the effect of vitamin K in coagulation factor synthesis. This should be considered in patients with blood coagulation disorders or suspected vitamin K deficiency.

Special precautions for use

Caution should be exercised in administering intravenous fat emulsions in patients with metabolic acidosis, severe liver damage, pulmonary disease,

sepsis, disease of the reticuloendothelial system, anaemia or blood coagulation disorders or when there is danger of fat embolism.

Administration of Lipofundin MCT/LCT should be accompanied by simultaneous carbohydrate infusions making up to 40% (at least) of the total calorie intake. 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. Interactions with other medicinal products and other forms of interaction

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

4.6. Use in pregnancy and lactation

The safety of Lipofundin MCT/LCT during pregnancy and lactation has not been assessed, but its use during these periods is not considered to constitute a hazard. Nevertheless, medicines should not be used in pregnancy, especially during the first trimester, unless the expected benefit is thought to outweigh any possible risk to the foetus.

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, leucopenia, 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.

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.

4.9. Overdose

In the event of an 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 patients and institute appropriate corrective measures.

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.

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 lecithin, 12.0 g/l
all-rac- α -tocopherol, 170 \pm 40 mg/l
Sodium oleate

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.

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 and other handling

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 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 emulsion 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.

Use only if the emulsion is homogenous, milky white and the container is undamaged. Inspect the emulsion visually for phase separation prior to administration.

7 MARKETING AUTHORISATION HOLDER

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