**Directions for Use**
B. Braun Melsungen AG · 34209 Melsungen, Germany

# Lipidem Emulsion for Infusion

## Composition

1000 ml emulsion contains:

*Active substances*

| | |
|---|---|
| Medium-chain triglycerides | 100.0 g |
| Soya-bean oil, refined | 80.0 g |
| Omega-3-acid triglycerides | 20.0 g |

*Excipients*
Egg lecithin, glycerol, sodium oleate, ascorbyl palmitate, all-rac-α-tocopherol, sodium hydroxide, water for injections.

Content of essential fatty acids per 1000 ml:

| | |
|---|---|
| Linoleic acid (omega-6) | 48.0 – 58.0 g |
| Alpha-linolenic acid (omega-3) | 5.0 – 11.0 g |
| Eicosapentaenoic acid and docosahexaenoic acid (omega-3) | 8.6 – 17.2 g |

## Pharmaceutical form

Emulsion for infusion
white, homogeneous emulsion

| | |
|---|---|
| Total energy per liter | 7900 kJ/l ≙ 1910 kcal/l |
| Osmolality | approximately 410 mOsm/kg |
| Titration (to pH 7.4) | less than 0.5 mmol/l NaOH or HCl |
| pH | 6.5 – 8.5 |

## Indications

Supply of lipids, including essential omega-6 fatty acids and omega-3 fatty acids, as part of a parenteral nutrition regimen for adults, when oral or enteral nutrition is impossible, insufficient or contra-indicated.

## Contraindications

Lipidem must not be used in any of the following conditions:
- severe hyperlipidemia
- severe blood coagulation disorders
- intrahepatic cholestasis
- severe liver failure
- severe renal failure without access to haemofiltration or dialysis.
- acute phase of myocardial infarction or stroke
- acute thromboembolic disease, lipid embolism
- hypersensitivity to egg, fish, or soya-bean protein or to any of the active substances or excipients.

The following conditions are general contraindications to infusion therapy:
- unstable hemodynamic status with compromised vital functions (conditions of collapse and shock)
- unstable metabolic conditions (e.g. severe post-traumatic conditions, uncompensated diabetes mellitus, severe sepsis, acidosis)
- acute pulmonary edema
- hyperhydration
- decompensated cardiac insufficiency
- hypotonic dehydration
- hypokalaemia.

## Special warnings and precautions for use

Serum triglycerides should be monitored during the infusion of Lipidem. In patients with suspected disorders of lipid metabolism, fasting lipemia should be ruled out before the start of the infusion. Hypertriglyceridemia 12 hours after the administration of lipids is also indicative of abnormal lipid metabolism.

Transient hypertriglyceridemia or elevated blood glucose levels may arise, depending on the patient's metabolic status. If the plasma triglyceride concentration rises to more than 3 mmol/l during administration of the lipid emulsion, it is recommended to reduce the infusion rate. If the plasma triglyceride concentration remains higher than 3 mmol/l, the infusion should be stopped until the plasma triglyceride concentration is normalized.

Electrolytes, fluid balance or body weight, acid-base balance, blood glucose levels, and, during long-term administration, full blood counts, coagulation status, and liver function should be monitored.

Infusion of Lipidem should be discontinued in case of appearance of any sign of allergic reaction, e.g. fever, shivering, rash, dyspnoea.

An overdose may lead to fat overload syndrome (see section 'Undesirable effects').

There is as yet no clinical experience of the use of Lipidem in children and adolescents, and there is only limited experience of its use in patients with diabetes mellitus or renal failure.

There is as yet only limited experience of the use of Lipidem for periods longer than seven days.

Caution should be exercised in patients with conditions associated with disturbed lipid metabolism, such as renal insufficiency, diabetes mellitus, pancreatitis, hepatic insufficiency, hypothyroidism (in the presence of hypertriglyceridemia), pulmonary disease and sepsis.

Lipids may interfere with certain laboratory tests (such as bilirubin, lactate dehydrogenase, oxygen saturation, haemoglobin measurement) when the blood sample is taken before the lipids have been eliminated from the bloodstream. In most patients the lipids are eliminated within 5 to 6 hours after the end of the infusion.

Energy supply with lipid emulsions only could cause metabolic acidosis. This may be avoided by the concurrent administration of carbohydrates. It is therefore recommended to infuse an adequate quantity of intravenous carbohydrates or carbohydrate-containing amino acid solutions along with the fat emulsion.

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

Lipidem contains 2.6 mmol/l of sodium. This should be taken into consideration by patients on a controlled sodium diet.

## Interactions

Heparin induces a transient release of lipoprotein lipase into the bloodstream. This may initially lead to increased plasma lipolysis, followed by a transient decrease in triglyceride clearance.

Soya-bean oil has a natural content of vitamin $K_1$. The content is however so low in Lipidem that it is not expected to significantly influence the coagulation process in patients treated with coumarin derivatives. Nevertheless, the coagulation status should be monitored in patients treated concomitantly with anticoagulants.

## Pregnancy and lactation

*Pregnancy*

There is no experience of the use of Lipidem in pregnant women. Parenteral nutrition may become necessary during pregnancy. Lipidem should only be given to pregnant women after careful consideration.

*Lactation*

There is no experience of the use of Lipidem in nursing mothers. It is as yet not known if Lipidem crosses the placental barrier or is excreted in breast milk. No respective data are available from animal experiments either. Breast-feeding is in general not recommended to mothers on parenteral nutrition.

## Posology and method of administration

**Adults:**

Dosage should be adjusted to the individual patient's needs.

B BRAUN

schwarz
Dokument = 210 x 297 mm
2 Seiten
Lätus
113
LIPIDEM
418/12605052/1208 – englisch
Standort Melsungen
G081658

*Recommended dosage:*
1 – 2 g fat per kg body weight per day, equivalent to:
5 – 10 ml of Lipidem per kg body weight per day

*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.

*Maximum infusion rate:*
Up to 0.15 g lipids per kg body weight per hour, equivalent to:
up to 0.75 ml of Lipidem per kg body weight per hour
The infusion rate should be reduced in undernourished patients.

**Paediatric patients:**

Safety and efficacy in children and adolescents have not been established (see section 'Special warnings and precautions for use').

*Duration of use*
As clinical experience with long-term use of Lipidem is limited, it should normally not be administered for longer than one week. Only if clearly needed the emulsion may be administered longer, with careful metabolic monitoring.

*Method of administration*
Intravenous use. Lipidem is suitable for both central and peripheral intravenous infusion.

**Overdose**

Overdose leading to fat overload syndrome may occur as a result of a too rapid infusion rate, or chronically at recommended rates of infusion in association with a change in the patients clinical conditions e.g. renal function impairment or infection. Overdosage may lead to undesirable effects (see section 'Undesirable effects').

Substantial overdosage with a fat emulsion that contains medium-chain triglycerides may lead to metabolic acidosis, especially when no carbohydrates are given concomitantly.

*Treatment*
In case of an overdose, the infusion must be stopped immediately. Other therapeutic measures will depend on a patient's specific symptoms and their severity. If the infusion is restarted after symptoms have subsided, the infusion rate should be increased gradually with close monitoring.

**Undesirable effects**

The following undesirable effects include a number of systemic reactions that are very rarely associated with the use of Lipidem:

**Blood and lymphatic system disorders**

Very rare (<1/10,000): Hypercoagulation

**Immune system disorders**

Very rare (<1/10,000): Allergic reactions

**Metabolic and nutritional disorders**

Very rare (<1/10,000): Hyperlipidemia, hyperglycemia, metabolic acidosis, ketoacidosis
The frequency of these undesirable effects is dose-dependent. They are likely to occur as symptoms of absolute or relative overdose. The frequency applies to conditions of correct use in terms of dosage, monitoring, observation of safety restrictions and further instructions.

**Central and peripheral nervous system disorders**

Very rare (<1/10,000): Drowsiness

**Vascular disorders**

Very rare (<1/10,000): Hypertension or hypotension

**Respiratory, thoracic and mediastinal disorders**

Very rare (<1/10,000): Dyspnea, cyanosis

**Gastrointestinal disorders**

Very rare (<1/10,000): Nausea, vomiting

**General disorders and/or administration site conditions**

Very rare (<1/10,000): Headache, flushing / erythema, elevated body temperature, sweating, chills, chest and back pain, fat overload syndrome (see below).

Should these undesirable effects occur or should the triglyceride level rise above 3 mmol/l during infusion, the infusion of Lipidem 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.

Triglycerides that contain omega-3 fatty acids may increase bleeding time and inhibit platelet aggregation. In patients with aspirin-induced asthma, pulmonary function may deteriorate as well.

Lipidem should always be a part of a complete parenteral nutritional treatment including amino acids and glucose. Nausea, vomiting, lack of appetite and hyperglycemia are symptoms related to conditions indicating parenteral nutrition and may sometimes 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 hypertriglyceridemia, 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 hyperlipemia, fever, fat infiltration, hepatomegaly with or without icterus, splenomegaly, anemia, leukopenia, thrombocytopenia, coagulation disorder, hemolysis 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 Lipidem should be discontinued immediately.

**Expiry date**

The product must not be used after the expiry date printed on the container.

**Instructions for storage /use/ handling**

Keep out of the reach and sight of children.

Do not store above 25 °C. Store in the original package in order to protect from light. Do not freeze. Products that have been frozen should be discarded.

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

Use only if the emulsion is homogeneous from intact containers. Inspect the emulsion visually for phase separation prior to administration.

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

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).

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

**Date of revision of the text**

11.2008

**B. Braun Melsungen AG**
34209 Melsungen, Germany