SMOFlipid 20 %
Soybean oil, Medium Chain triglycerides, Refined olive oil, Purified fish oil
Emulsion for Infusion

1000 ml contain:

- Soybean oil, refined: 60.0 g
- Medium chain triglycerides: 60.0 g
- Olive oil, refined: 50.0 g
- Purified fish oil, rich in omega 3 acids: 30.0 g
- Total energy: 8.4 MJ/l (=2000 kcal/l)
- pH-value: approx. 8
- Osmolality: approx. 380 mosm/kg

Pharmacodynamic properties
The fat emulsion has a particle size and biological properties similar to those of endogenous chylomicrons. The constituents of Smoflipid: soya-bean oil, medium-chain triglycerides, olive oil and fish oil have except for their energy contents, their own pharmacodynamic properties. Soya-bean oil has a high content of essential fatty acids. The omega 6 fatty acid linoleic acid is the most abundant (approx. 55-60%). Alpha-linolenic acid, an omega 3 fatty acid, constitutes about 8%. This part of Smoflipid provides the necessary amount of essential fatty acids. Medium-chain fatty acids are rapidly oxidized and provide the body with a form of immediately available energy. Olive oil mainly provides energy in the form of mono-unsaturated fatty acids, which are much less prone to peroxidation than the corresponding amount of poly-unsaturated fatty acids. Fish oil is characterised by a high content of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). DHA is an important structural component of cell membranes, whereas EPA is a precursor of eicosanoida as prostaglandin, thromboxanes and leucotrienes. Vitamin E protects unsaturated fatty acid against lipid peroxidation.

Pharmacokinetic properties
The individual triglycerides have different clearance rate but Smoflipid as a mixture is eliminated faster than long chain triglycerides (LCT) with lower triglyceride levels during infusion. Olive oil has the slowest clearance rate of the components (somewhat slower than LCT) and medium chain triglycerides (MCT) the fastest. Fish oil in a mixture with LCT has the same clearance rate as LCT alone.

Preclinical safety data
In pre-clinical studies no other effects than those expected after high doses of lipids were observed, based on single dose and repeat dose toxicity and genotoxicity studies performed with the Smoflipid emulsion. In a local tolerance study in rabbits a slight, transient inflammation after intra-arterial, paravenous or subcutaneous administration a moderate transient inflammation and tissue necrosis were seen in some animals.

In a test in guinea pig (maximisation test) fish oil showed moderate dermal sensitisation. A systemic antigenicity test gave no indication of evidence of anaphylatic potential of fish oil.

Indications
To supply energy and essential fatty acids and omega-3 fatty acids to adults, as part of a parenteral nutrition regimen, when oral or enteral nutrition is impossible, insufficient or contra-indicated.

Contraindications
- Hypersensitivity to fish-, egg- or soy protein or to any of the active substances or excipients.
- Severe hyperlipidemia.
- Severe liver insufficiency.
- Severe blood coagulation disorders.
- Severe renal insufficiency without access to hemofiltration or dialysis.
- Acute shock
- General contraindications to infusion therapy: acute pulmonary oedema, hyperhydration, decompensated cardiac insufficiency.
- Unstable conditions (e.g. severe post-traumatic conditions, uncompensated diabetes mellitus, acute myocardial infarction, stroke, embolism, metabolic acidosis and severe sepsis and hypotonic dehydration).

Special warnings and special precautions for use
The capacity to eliminate fat is individual and should therefore be monitored according to the routines of the clinician. This is in general done by checking the triglyceride levels. The concentration of triglycerides in serum should not exceed 3 mmol/l during infusion. An overdose may lead to fat overload syndrome. At present there is no experience of SMOFlipid treatment for more than 14 days.

Smoflipid should be given with caution in conditions of impaired lipid metabolism, which may occur in patients with renal failure, diabetes mellitus, pancreatitis, impaired liver function, hypothyroidism, and sepsis. Clinical data in patients with diabetes mellitus or renal failure are limited. Administration of medium-chain fatty acids alone can result in metabolic acidosis. The risk is to a great extent eliminated by simultaneous infusion of the long chain fatty acids included in Smoflipid. Concomitant administration of carbohydrates will further eliminate this risk. Hence, simultaneous infusion of carbohydrate or a carbohydrate-containing amino acid solution is recommended. Laboratory test generally associated with monitoring of intravenous nutrition should be checked regularly. These include blood glucose levels, liver functions tests, acid base metabolism, fluid balance, full blood count and electrolytes. Any sign or symptoms of anaphylactic reaction (such as fever, shivering, rash or dyspnoea) should lead to immediate interruption of the infusion. High levels of lipids in plasma may interfere with some laboratory blood tests, e.g. haemoglobin. The addition of other medicaments or substances to smoflipid should generally be avoided unless compatibility is known.

Interaction
Heparin given in clinical doses causes a transient increase in lipoprotein lipase release into the circulation. This may initially result in increased plasma lipolysis followed by a transient decrease in triglyceride clearance. Soy-bean oil has a natural content of vitamin K1. The content is however so low in SMOFlipid that it is not expected to significantly influence the coagulation process in patients treated with coumarin derivatives.

Pregnancy and lactation
There are no data available on exposure of Smoflipid in pregnant or breast-feeding women. There are no studies available on reproductive toxicity in animals. Smoflipid should only be given to pregnant and breast-feeding women after careful consideration.

Driving and using machines
No effects on the ability to drive and operate machines are to be expected.

Dosage and administration
Dosage
Adults
The standard dose is 1.0-2.0 g fat/kg body weight/day, corresponding to 5-10 ml/kg b.w./day. The recommended infusion rate of 0.125 g fat/kg b.w./hour, corresponding to 0.63 ml SMOFlipid/kg b.w./hour, and should not exceed 0.15 g fat/kg b.w./hour, corresponding to 0.75 ml SMOFlipid/kg b.w./hour.

Paediatric patients
At present there is no experience with SMOFlipid in paediatric patients. Use in paediatric patients is therefore not recommended.
**Administration**
Intravenous infusion into a peripheral or central vein.

**Instructions for use and handling**
Use only if the emulsion is homogenous. Inspect the emulsion visually for phase separation prior to administration. Ensure that the final emulsion for infusion does not show any evidence of phase separation. For single use only.
Any unused emulsion should be discarded.

**Additives**
SMOFlipid may be aseptically admixed with amino acid, glucose, and electrolyte solutions to produce "All-In-One" Total Parenteral Nutrition (TPN) admixtures.
Compatibility for different additives and the storage time of the different admixtures will be available upon request from marketing authorisation holder.
Additions should be made aseptically.
Any mixture remaining after infusion must be discarded.

**Undesirable effects**
Undesirable effects observed during the administration of fat emulsions:

<table>
<thead>
<tr>
<th>Common &gt; 1/100 &lt;1/10</th>
<th>Uncommon &gt; 1/1000, &lt;1/100</th>
<th>Rare &gt; 1/10000, &lt;1/1000</th>
<th>Very rare &lt;1/10000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vascular disorders</td>
<td>Hypotension</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td>Dyspnoea</td>
<td></td>
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<tr>
<td>Gastrointestinal disorders</td>
<td>Lack of appetite, nausea, vomiting</td>
<td></td>
<td></td>
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<tr>
<td>Reproductive system and breast disorders</td>
<td></td>
<td></td>
<td>Priapism</td>
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<tr>
<td>General disorders and administration site conditions</td>
<td>Slight increase in body temperature</td>
<td>Chills</td>
<td>Hipersensitivity reactions (e.g. anaphylactic or anaphylactoid reactions, skin rash, urticatia, flush, headache), heat or cold sensation, paleness, cyanosis, pain in the neck, back, bones, chest, and joins.</td>
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</tbody>
</table>
**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, in association with a sudden change in the patient's clinical condition, such as renal function impairment or infection. The fat overload syndrome is characterized by hyperlipidemia, fever, fat infiltration hepatomegaly, with or without icterus, splenomegaly, anemia, leukopenia, thrombocytopenia, coagulation disorder, hemolysis and reticulocytosis, abnormal liver function test and coma. The symptoms are usually reversible if the infusion of the fat emulsions is discontinued.

Should signs of a fat overload syndrome occur, the infusion of Smoflipid should be discontinued.

**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 is association with a change in the patients clinical conditions e.g. renal function impairment or infection.

Overdosage may lead to side-effects. In these cases the lipid infusion should be stopped or, if necessary, continued at a reduced dosage.

**Storage**

Do not store above 25°C. Do not freeze.

**Storage after mixing**

If additions are made to Smoflipid, the admixtures should be done aseptically and should be used immediately from a microbiological point of view.

**Shelf life**

2 years

**Marketing Authorisation Holder**

Fresenius Kabi AB
75174 Uppsala, Sweden

**Pack sizes:**

- 10 x 100 ml  No Reg : DKI0774501749A1
- 10 x 250 ml  No Reg : DKI0774501749A1
- 10 x 500 ml  No Reg : DKI0774501749A1

**Harus dengan resep dokter**

**Manufactured by:**

Fresenius Kabi Austria GmbH, Graz, Austria for Fresenius Kabi AB 75174 Uppsala, Sweden

**Imported by:**

Fresenius Kabi Indonesia
Jakarta-Indonesia