Package Insert

SMOFlipid 20%

Emulsion for Infusion

1000 ml contain:

Soya-bean oil, refined	60.0 g
Medium-chain triglycerides	60.0 g
Olive oil, refined	50.0 g
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 H_2O

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

Contraindications
- Hypersensitivity to fish-, egg-, soya or peanut 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 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. Special caution should be taken in patients with a marked risk for hyperlipidemia (e.g. patients with high lipid dosage, severe sepsis and extremely low birth weight infants). The concentration of triglycerides in serum should in general not exceed 3 mmol/l during infusion. An overdose may lead to fat overload syndrome.

This medicinal product contains soya-bean oil, fish oil and egg phospholipids, which may rarely cause allergic reactions. Cross allergic reaction has been observed between soya-bean and peanut.

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. This risk is to a great extent eliminated by the 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 symptom of anaphylactic reaction (such as fever, shivering, rash or dyspnoea) should lead to immediate interruption of the infusion.

Smoflipid should be given with caution to neonates and premature neonates with hyperbilirubinemia and cases with pulmonary hypertension. In neonates, particularly premature neonates on long term parenteral nutrition, blood platelet counts, liver function tests and serum triglycerides should be monitored.

Light exposure of solutions 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 neonates and children below 2 years, Smoflipid should be protected from ambient light until administration is completed (see Dosage and administration, Storage and Shelf life and Instruction for use and handling).

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.

Soya-bean oil has a natural content of vitamin K_1. 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. Parenteral nutrition may become necessary during pregnancy and lactation. 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
The patient's ability to eliminate the fat infused, should govern the dosage and infusion rate, see section "Special warning and precautions for use". Safety and efficacy of SMOFlipid treatment have been investigated in two randomized, controlled clinical trials (n=101) up to 4 weeks of treatment

Adults

The standard dose is 1.0 – 2.0 g fat/kg body weight (b.w.)/day, corresponding to 5 – 10 ml/kg b.w./day.
The recommended infusion rate is 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.

Neonates and infants

The initial dose should be 0.5 – 1.0 g fat/kg b.w./day followed by a successive increase by 0.5 – 1.0 g fat/kg b.w./day up to 3.0 g fat/kg b.w./day.

It is recommended not to exceed a daily dose of 3 g fat/kg b.w./d, corresponding to 15 ml Smoflipid/kg b.w./day.

The rate of infusion should not exceed 0.125 g fat/kg b.w./hour.
In premature and low birthweight neonates, Smoflipid should be infused continuously over about 24 hours.

When used in neonates and children below 2 years, the solution (in bags and administration sets) should be protected from light exposure until administration is completed (see Special warnings and precautions for use, Storage and Shelf life and Instruction for use and handling).

Children

It is recommended not to exceed a daily dose of 3 g fat/kg b.w./d, corresponding to 15 ml Smoflipid/kg b.w./day.

The daily dose should be increased gradually during the first week of administration.

The infusion rate should not exceed 0.15 g fat/kg b.w./hour.

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

	Common (≥1/100 to <1/10)	*Uncommon (≥1/1000 to <1/100)*	*Rare (≥1/10000 to <1/1000)*	*Very rare (<1/10000)*
Vascular disorders			Hypotension, hypertension	
Respiratory, thoriacic and mediastinal disorders			Dyspnoea	
Gastrointestinal disorders		Lack of appetite, nausea, vomiting		
Reproductive system and breast disorders				Priapism
General disorders and administration site conditions	Slight increase in body temperature	Chills	Hypersensitivity-reactions (e.g. anaphylactic or anaphylactoid reactions, skin rash, urticaria, fl headache), heat or cold sensation, paleness, cyanosis, pain in the neck, back, bones, chest and loins	

Administration

Intravenous infusion into a peripheral or central vein.

Should these side-effects occur or should the triglyceride level during infusion rise above 3 mmol/l, the infusion of Smoflipid should be stopped or, if necessary, continued at a reduced dosage.

Smoflipid should always be a part of a complete parenteral nutritional treatment including amino acids and glucose. Nausea, vomiting and hyperglycemia are symptoms related to conditions indicating parenteral nutrition and may sometimes be associated with parenteral nutrition.

Monitoring of triglycerides and blood glucose levels are recommended to avoid elevated levels, which may be harmful.

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

Overdosage may lead to side-effects (see section Undesirable effects, Fat overload syndrome). In these cases the lipid infusion should be stopped or, if necessary, continued at a reduced dosage.

Storage and Shelf life
Do not store above 25°C. Do not freeze.
Do not use after the expiry date stated on the label.
Keep out of reach and sight of children.

List of excipients
Glycerol
Egg lecithin
all-rac-Tocopherol
Water for injections
Sodium hydroxide for pH adjustment
Sodium oleate

Incompatibilities
This medicinal product must not be mixed with other medicinal products except those mentioned in section Additives.

Stability after mixing

If additions are made to Smoflipid, the admixtures should be used immediately from a microbiological point of view. If admixtures are not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2-8°C, unless additions have taken place in controlled and validated aseptic conditions.

When used in neonates and children below 2 years, the solution (in bags and administration sets) should be protected from light exposure until administration is completed (see Special warnings and precautions for use, Dosage and administration and Instruction for use and handling).

Instructions for use and handling

Use only if the emulsion is homogeneous.

When used in neonates and children below 2 years, protect from light exposure, until administration is completed. Exposure of Smoflipid to ambient 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 Special warnings and precautions for use, Dosage and administration and Storage and Shelf life).

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 the marketing authorisation holder.

Additions should be made aseptically.

Any mixture remaining after infusion must be discarded.

Pack sizes

Infusion bottle, glass bottles: 100 ml, 250 ml, 500 ml

10x100 ml, 10x250 ml, 10x500 ml

Marketing Authorisation holder
Fresenius Kabi AB, Uppsala, Sweden

Manufactured by:
Fresenius Kabi Austria GmbH, Graz, Austria
January 2020

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