Product name:		Territory:
SMOFlipid 20%		**ID**
Type of packaging:	Dosage:	
PIL	**50/100/250 ml**	
Material number:	2-D-Matrix-Code:	
M080176/04 ID	**M080176/04 ID**	
Pharma-Code (Laetus):	EAN-Code:	
-	**-**	
Dimension:	Font:	Size:
180 x 294 mm	**Interstate**	**7**

Colours:		
• **Black**	1. Draft	**10.03.2022, 13.45**
• **Die cut**	1. Corr	**02.05.2022, 14.45**
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Operator:
Peter Schaffer

SMOFlipid 20 %

Soya-bean oil, Medium chain triglycerides, Refined olive oil, Purified fish oil
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
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 characterized 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 eicosanoids as prostaglandins, thromboxanes and leucotrienes.
Vitamin E protects unsaturated fatty acids against lipid peroxidation.
Exploratory studies have been conducted in infants and children but confirmatory pivotal studies have not been provided. Twenty eight infants and children aged from 5 months to 2 years and from 2 to 11.5 years with stable disease requiring parenteral nutrition for at least 4 weeks received SMOFlipid or Intralipid 20% in a randomized, double-blind study. SMOFlipid or Intralipid were to be given as approx. 2 g fat/kg/day over 12-14 hours for 4-5 days per week with a recommended infusion rate of 0.125 g fat/kg/hour to a maximum of 0.15 g fat/kg/hour.
Oral/enteral intake was to be no more than 50% of caloric intake. Additional parenteral nutrition (amino acids and glucose) varied, dependent on patient total body weight. Efficacy was assessed by the fatty acid profile in plasma lipoproteins and RBC phospholipids and by body weight, height and body mass index. Changes from baseline in fatty acid concentrations in plasma lipoproteins or RBC phospholipids showed increased in EPA and DHA in patients given SMOFlipid compared with those given Intralipid. Small increases in weight, height and BMI were seen in both groups over the 4 week period.

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 preclinical 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 (maximization test) fish oil showed moderate dermal sensitization. A systemic antigenicity test gave no indication of evidence of anaphylactic potential of fish oil.

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 contraindicated.

Contraindications
- Hypersensitivity to fish-, egg- , soy 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 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. 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. Reduction of the dosage or cessation of the lipid emulsion should be considered if serum or plasma triglyceride concentrations during or after infusion exceed 3 mmol/L. 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, pancreatic, 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 results 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.

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.

Effects on laboratory tests
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.
As with all lipid emulsions, SMOFLipid may interfere with certain laboratory measurements (bilirubin, haemoglobin, lactate dehydrogenase, oxysaturation), if blood is sampled before fat has adequately been cleared from the blood stream. In most patients, fat is cleared after a fat free period or interval of 5 to 6 hours.

Paediatric use
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 Instruction for use and handling).

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.

Use in pregnancy
There are no adequate and well-controlled studies in pregnant women with SMOFlipid or its individual components; therefore the safety of SMOFlipid in pregnant women is not known. No animal studies have been conducted with the combined lipid components of SMOFlipid to evaluate effects on reproduction. Possible embryotoxic effect was evidenced by a slight increase in embryonic/foetal loss in rabbits that had received medium chain fatty acid-containing lipids similar to SMOFlipid during the period of organogenesis, at a dose 3 and 7.5 times the maximum clinical dose and infusion rate, the embryotoxicity is most likely related to the high maternal systemic exposure of medium-chain fatty acids (MCFA).
SMOFlipid should not be used during pregnancy unless the expected therapeutic benefit clearly outweighs the potential risk to the fetus.

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Use in lactation
It is not known whether SMOFlipid can enter maternal milk. Therefore, SMOFlipid should be used during lactation only if clearly needed.

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

Dosage and administration
Dosage

The patient's ability to eliminate the fat infused, should govern the dosage and infusion rate, see **Special warnings and special precautions for use.**

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.

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 special precautions for use, Storage 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.

Administration
Intravenous infusion into a peripheral or central vein.

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 special precautions for use, Dosage and administration and Storage).

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 authorization 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 :

	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			dyspnea	
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	heat or cold sensation, paleness, cyanosis, pain in the neck, back, bones, chest and loins	
Immune system disorders			Hypersensitivity-reactions (e.g. anaphylactic or anaphylactoid reactions, skin rash, urticaria, flush, headache)	

Should these side-effects occur or should the triglyceride level during infusion rise about 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, 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, leucopenia, 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 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
Store below 25°C (Under controlled air conditioning). 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.
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 special precautions for use, Storage and Instruction for use and handling).

Shelf life
2 years

Pack sizes :
Bottle @ 50 ml No. Reg : DKI0774501749A1
Bottle @ 100 ml No. Reg : DKI0774501749A1
Bottle @ 250 ml No. Reg : DKI0774501749A1

Harus dengan resep dokter
On medical prescription only.

Manufactured by :
Fresenius Kabi Austria GmbH, Graz, Austria for
Fresenius Kabi AB, 75174 Uppsala, Sweden

Imported by :
Fresenius Kabi Combiphar
Bandung Barat – Indonesia

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