APPROVED PROFESSIONAL INFORMATION

SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

SMOFlipid 20 % Emulsion for intravenous infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 000 ml contains:

Soybean 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 (= 2 000 kcal/l)

Sugar free.

Excipients with known effect:

1000 ml emulsion contains up to 5 mmol sodium (as sodium hydroxide and sodium oleate).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Emulsion for intravenous infusion

A white homogenous emulsion

pH value: ± 8

Osmolality: ± 380 mOsm/kg

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

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

4.2 Posology and method of administration

Posology

The patient's ability to eliminate the fat infused, should govern the dosage and infusion rate.

Adults

The standard dose is 1,0 to 2,0 g fat/kg body weight/day, corresponding to 5-10 ml/kg body weight/day.

The infusion rate of 0,125 g fat/kg body weight/hour, corresponding to 0,63 ml SMOFlipid/kg body weight/hour, is recommended and should not exceed 0,15 g fat/kg body weight/hour, corresponding to 0,75 ml SMOFlipid/kg body weight/hour.

Neonates and infants

The initial dose should be 0,5 – 1,0 g fat/kg body weight/day followed by a successive increase by 0,5 – 1,0 g fat/kg body weight/day up to 3,0 g fat/kg body weight/day.

It is recommended not to exceed a daily dose of 3 g fat/kg body weight/day, corresponding to 15 ml SMOFlipid/kg body weight/day.

The rate of infusion should not exceed 0,125 g fat/kg body weight/hour.

In premature and low birth weight neonates, SMOFlipid should be infused continuously over about 24 hours.

Children

It is recommended not to exceed a daily dose of 3 g fat/kg body weight/day, corresponding to 15 ml SMOFlipid/kg body weight/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 body weight/hour.

Method of administration

For intravenous infusion into a peripheral or central vein.

4.3 Contraindications

- Hypersensitivity to fish, egg, soya or peanut protein or to any of the active substances or excipients listed in section 6.1
- Severe hyperlipidaemia
- Severe liver insufficiency
- Severe blood coagulation disorders
- Severe renal insufficiency without access to haemofiltration or dialysis
- Acute shock
- General contraindications to infusion therapy: acute pulmonary oedema, fluid overload, decompensated cardiac insufficiency
- Unstable conditions (e.g. severe post-traumatic conditions, uncompensated diabetes mellitus, acute myocardial infarction, stroke, embolism, metabolic acidosis, severe sepsis and hypotonic dehydration).

4.4 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 hyperlipidaemia (e.g. patients with high lipid dosage and severe sepsis). The concentration of triglycerides in serum should 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, see section 4.8.

SMOFlipid 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. 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 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 tests generally associated with monitoring of intravenous nutrition should be checked regularly. These include blood glucose levels, liver function tests, acid base metabolism, fluid balance, full blood count and electrolytes.

SMOFlipid should be given with caution to neonates and premature neonates with hyperbilirubinaemia 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 sections 6.3 and 6.6).

High levels of lipids in plasma may interfere with some laboratory blood tests, e.g. haemoglobin. Monitoring of triglycerides and blood glucose levels are recommended to avoid elevated levels, which may be harmful.

At present there is limited experience of SMOFlipid treatment for more than 14 days.

SMOFlipid contains up to 5 mmol sodium per 1 000 ml. To be taken into consideration by patients on a controlled sodium diet.

The addition of other medicines or substances to SMOFlipid should generally be avoided unless compatibility has been proven (see sections 6.2 and 6.6).

4.5 Interaction with other medicines and other forms of 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.

Soybean 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.

4.6 Fertility, pregnancy and lactation

There are no data available on the use of SMOFlipid in pregnant or breastfeeding women. There are no studies available on reproductive toxicity in animals. SMOFlipid should only be given to pregnant and breastfeeding women after careful consideration.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

a. Summary of the safety profile

No information available.

b. Tabulated list of adverse reactions

Frequencies are defined as:

Common (≥ 1/100 to < 1/10)

Uncommon (≥ 1/1 000 to < 1/100)

Rare (≥ 1/10 000 to < 1/1 000)

Very rare (< 1/10 000)

Vascular disorders

Rare: Hypotension, hypertension

Respiratory, thoracic and mediastinal disorders

Rare: Dyspnoea

Gastrointestinal disorders

Uncommon: Lack of appetite, nausea, vomiting

Reproductive system and breast disorders

Very rare: Priapism

General disorders and administration site conditions

Common: Slight increase in body temperature

Uncommon: Chills

Immune system disorders

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

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 hyperglycaemia are symptoms related to conditions indicating parenteral nutrition and may sometimes be associated with parenteral nutrition.

c. Description of selected adverse reactions

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 hypertriglyceridaemia, 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 hyperlipidaemia, fever, fat infiltration, hepatomegaly with or without icterus, splenomegaly, anaemia, leukopenia, thrombocytopenia, coagulation disorders, haemolysis 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.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the “6.04 Adverse Drug Reactions Reporting Form”, found online under SAHPRA’s publications: https://www.sahpra.org.za/Publications/Index/8.

4.9 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 patient’s clinical conditions e.g. renal function impairment or infection.

Overdosage may lead to side effects (see section 4.8). In these cases, the lipid infusion should be stopped or, if necessary, continued at a reduced dosage.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 25.6 Other special foods

Pharmacotherapeutic group: Solutions for parenteral nutrition, fat emulsions

ATC-code: B05BA02

The fat emulsion has a particle size and biological properties similar to those of endogenous chylomicrons. The constituents of SMOFlipid: soybean oil, medium-chain triglycerides, olive oil and fish oil have, except for their energy contents, their own pharmacodynamic properties.

Soybean oil has a high content of essential fatty acids. The omega-6 fatty acid linoleic acid is the most abundant (± 55 - 60 %). Alpha-linoleic 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 oxidised 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 eicosanoids as prostaglandins, tromboxanes and leukotrienes.

Vitamin E protects unsaturated fatty acids against lipid peroxidation.

5.2 Pharmacokinetic properties:

The individual triglycerides have different clearance rates, 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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Egg lecithin

Glycerol

Sodium oleate

Sodium hydroxide (for pH-adjustment)

Antioxidant: DL-α-Tocopherol (~ 0,02 % *m/v)*

Water for injections

6.2 Incompatibilities

SMOFlipid must not be mixed with other medicinal products except those mentioned in section 6.6.

6.3 Shelf life

2 years

Shelf life after first opening the container:

Chemical and physical in-use stability has been demonstrated for 24 hours at 25 °C. From a microbiological point of view the product should be used immediately. If not used immediately, the 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.

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 sections 4.4 and 6.6).

6.4 Special precautions for storage

Store at or below 25 °C. Do not freeze.

Storage 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, the 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.

6.5 Nature and contents of container

The clear glass bottles are packed with a professional information leaflet into outer cardboard cartons as follows:

10 x 100 ml, 10 x 250 ml, 10 x 500 ml.

Although the above pack sizes are available from the manufacturer, not all pack sizes may be marketed in this country.

6.6 Special precautions for disposal and other handling

Use only if the emulsion is homogenous.

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 sections 4.4 and 6.3).

Additives

SMOFlipid may be aseptically mixed with amino acids, glucose, and electrolyte solutions to produce “All-in-one” total parenteral nutrition (TPN) admixtures.

Additions should be made aseptically.

Any mixture remaining after infusion must be discarded.

7. HOLDER OF THE CERTIFICATE OF REGISTRATION

Fresenius Kabi South Africa (Pty) Ltd

Stand 7, Growthpoint Business Park

162 Tonetti Street

Halfway House, Midrand, 1685

South Africa

8. REGISTRATION NUMBER

41/25.2/0060

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

12 June 2009

10. DATE OF REVISION OF THE TEXT

28 October 2022