

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

STRUCTOLIPID 20% emulsion for infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

100 ml of the emulsion contains

Active ingredient	Quantity
Purified structured triglyceride	20 g

For the full list of excipients, see section 6.1

The active ingredient, purified structured triglyceride, can be defined as an interesterified mixture of equimolar amounts of long chain triglycerides (LCT) and medium chain triglycerides (MCT), corresponding to 64% (w/w) and 36% (w/w), respectively. The fatty acids are randomly distributed within the interesterified triglyceride molecule. Purified structured triglyceride consists mainly of mixed chain triglycerides, i.e. containing medium as well as long chain fatty acids (approx 75%) with minor proportions of LCT and MCT. MCT is a synthetic oil originated from coconut oil and/or palm kernel oil and LCT is added in the form of refined soybean oil.

Osmolality:	350 mosm/kg water
pH	Approx 8
Energy content:	8.2 MJ (1960 kcal) /1000 ml

3 PHARMACEUTICAL FORM

Emulsion for infusion

White homogenous emulsion

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

To supply energy and essential fatty acids to adult patients, as part of a parenteral nutrition regimen.

4.2 Posology and method of administration

The patient's ability to eliminate the fat infused, should govern the dosage and infusion rate, see 4.4, "Special warnings and special precautions for use".

Posology

Adults

The recommended dose is 1-1.5 g triglycerides/kg body weight/day, corresponding to 5-7.5 ml/kg body weight/day, normally given over 10-24 hours.

The infusion rate should not exceed 0.75 ml /kg body weight/ hour, corresponding to 0.15 g fat / kg body weight/ hour.

Paediatric population

Safety and efficacy in children have not been established.

Method of administration

STRUCTOLIPID should be administered by intravenous infusion as part of a parenteral nutrition regimen, including glucose, into a peripheral vein or via a central venous catheter.

4.3 Contraindications

Hypersensitivity to egg-, soya- or peanut protein, to any of the active substances or to any of the excipients listed in section 6.1

Severe hyperlipemia

Severe liver insufficiency

Hemophagocytotic syndrome

Severe blood coagulation disorders

Acute shock

General contra-indications of an infusion therapy: acute pulmonary oedema, hyperhydration and decompensated cardiac insufficiency.

4.4 Special warnings and precautions for use

Triglyceride concentrations in serum should be monitored. When disturbed fat metabolism is suspected, this should be done daily. The serum triglyceride concentration should not exceed 3 mmol/l during the infusion. The next infusion should only be started when serum triglyceride levels have returned to the baseline.

Blood glucose levels, serum electrolytes, liver function tests, fluid balance, and blood status should be monitored regularly. When acidosis is suspected or occurs, acid-base balance should be monitored as well.

This medicinal product contains soybean oil (in the form of purified structured triglycerides), which may rarely cause allergic reactions. Cross-allergic reactions have been observed between soybean and peanut.

Any sign or symptom of anaphylactic reaction (such as fever, shivering, rash or dyspnoea) should lead to immediate interruption of the infusion.

STRUCTOLIPID should be given with caution to patients with impaired lipid metabolism such as in renal insufficiency, uncontrolled diabetes mellitus, pancreatitis, impaired liver function, hypothyroidism (if hypertriglyceridemic) and sepsis.

There is at present no clinical experience of the use of STRUCTOLIPID in children and limited experience in patients with diabetes mellitus or renal failure.

STRUCTOLIPID should be administered simultaneously with carbohydrates to avoid the occurrence of metabolic acidosis.

STRUCTOLIPID may interfere with certain laboratory measurements (e.g. bilirubin, lactate dehydrogenase, oxygen saturation, Hb) if blood is sampled before fat has been adequately cleared from the bloodstream. Fat is cleared after a fat-free interval of 5-6 hours in most patients.

4.5 Interaction with other medicinal products and other forms of interaction

Some drugs, like insulin, may interfere with the body's lipase system. However, this kind of interaction seems to have little clinical significance.

Heparin given in clinical doses causes a transient release of lipoprotein lipase into the circulation. This may result initially in increased plasma lipolysis followed by a transient decrease in triglyceride clearance.

Soybean oil has a natural content of vitamin K₁. However, the concentration in STRUCTOLIPID is so low that it is not expected to significantly influence the coagulation process in patients treated with coumarin derivatives.

4.6 Fertility, pregnancy and lactation

Pregnancy

For STRUCTOLIPID no clinical data on exposed pregnancies are available. Structolipid has not been tested in animals for effects on the conceptus beyond the period of organogenesis. Evaluation of animal data has shown reproductive toxicity (see section 5.3). The clinical relevance of this data is unknown. STRUCTOLIPID should be used during pregnancy only after special consideration.

Breastfeeding

No clinical experience of use during breast-feeding is available. Women treated with STRUCTOLIPID should not breast-feed.

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

Structolipid infusion may cause a rise in body temperature and nausea, furthermore increases in serum-triglycerides and ketone bodies have been reported (incidence > 1% in clinical trials).

Reports of adverse events in conjunction with Structolipid infusion are extremely rare and have been predominantly noted during clinical studies.

	<i>Common</i> <i>≥1/100 to < 1/10</i>	<i>Uncommon</i> <i>≥1/1,000 to <1/100</i>	<i>Very rare</i> <i>< 1/10,000</i>
Metabolism and nutrition disorders	Hypertriglyceridaemia Ketosis		
Nervous system disorders			Dizziness
Cardiac disorders			Tachycardia Hypertension
Respiratory, thoracic and mediastinal disorders			Respiratory distress i.e. respiratory symptoms
Gastrointestinal disorders		Diarrhoea Vomiting	
Hepatobiliary disorders			Transient increase in liver function test
Skin and subcutaneous tissue disorders			Rash
Musculoskeletal and connective tissue disorders		Back pain	
General disorders and administration site conditions	Headache Nausea Rise in body temperature	Shivering	

Liver function tests may show increased levels during parenteral nutrition regardless of whether fat is included or not.

Fat overload syndrome

An impaired capacity to eliminate triglycerides may lead to the fat overload syndrome as a result of overdosage. However, this syndrome may appear also 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 characterised by hyperlipemia, fever, fat infiltration and disorders in various organs and coma. All symptoms are usually reversible if the infusion of the fat emulsion is discontinued.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system

[To be completed nationally]

4.9 Overdose

See 4.8, Undesirable effects, Fat overload syndrome

Severe overdose of fat emulsions containing MCT can, specially if carbohydrates are not administered simultaneously, lead to metabolic acidosis.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Solutions for parenteral nutrition, fat emulsions

ATC-code: B05BA02

Fat emulsion for intravenous nutrition STRUCTOLIPID is a fat emulsion with particle size and biological properties similar to those of endogenous chylomicrons. Unlike chylomicrons, STRUCTOLIPID does not contain cholesterol esters and apolipoproteins.

Another difference compared with chylomicrons is that STRUCTOLIPID is a mixture of long and medium chain fatty acids on the same glycerol molecule.

The emulsion provides both essential fatty acids (long chain fatty acids, LCFA) and energy substrate in the form of both LCFA and medium chain fatty acids (MCFA).

To prevent essential fatty acid deficiency, at least 20% of the nonprotein energy should be supplied in the form of fat emulsions with an adequate amount of linoleic and linolenic acid such as STRUCTOLIPID.

5.2 Pharmacokinetic properties

A study in healthy volunteers has shown that STRUCTOLIPID is eliminated faster than emulsions containing only triglycerides with long chain fatty acids.

Retrospectively analysed data from studies in patients suggest a faster elimination of STRUCTOLIPID than that of emulsions containing only LCT or a physical mixture of LCT and MCT.

Due to the metabolism of STRUCTOLIPID, increased plasma levels of medium chain fatty acids, dicarboxylic acids and 3-hydroxy fatty acids will be generated. Studies in healthy volunteers have

shown that the amounts of these metabolites are lower after infusion of STRUCTOLIPID compared with after infusion of equimolar doses of fat in a physical mixture of LCT and MCT. These metabolites were found to be completely eliminated in a blood sample drawn 16 hours after completion of the infusion. Dicarboxylic acids are excreted in the urine.

5.3 Preclinical safety data

Preclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity and genotoxicity. The carcinogenic potential of STRUCTOLIPID has not been evaluated.

No teratogenic or embryotoxic potential was evident in rabbits after infusions of STRUCTOLIPID at a dosage of 3 g (TG) /kg/day (0.75 g TG/kg/h) over 4 hours.

At a dosage of 4.5 g TG/kg/day (1.12 g TG/kg/h), a possible embryotoxic effect was evidenced by a slight increase in embryonic/fetal loss. The dosage and infusion rate were 3 and 7 times higher, respectively, than recommended for clinical use.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Purified egg phospholipids
Glycerol, Sodium hydroxide
Water for injections.

6.2 Incompatibilities

This medicinal product should not be mixed with other products than those mentioned in Section 6.6, unless full compatibility of Structolipid with the product has been demonstrated.

Additives may only be added to STRUCTOLIPID in cases where compatibility has been documented. The compatibility with solutions administered simultaneously via a common port (Y-connector) must be ensured.

6.3 Shelf-life

Shelf-life in the product as packaged for sale
2 years

Shelf-life after first opening the container

The emulsion should be used directly due to the risk of microbiological contamination. Any unused emulsion should be discarded.

Shelf-life after addition or mixing according to directions
See section 6.6, Stability

6.4 Special precautions for storage

Do not store above 25 °C. Do not freeze

6.5 Nature and content of container

The container consists of an inner bag and an overpouch. An oxygen absorber and integrity indicator are placed between the inner bag and the overpouch. The inner bag is the primary container for Structolipid. The overpouch provides protection during storage by contributing with barrier properties towards water and oxygen to the Structolipid container system. The oxygen absorber will absorb and bind oxygen remaining between the inner bag and the overpouch. The integrity indicator will react with free oxygen and change from clear to black in case of a damaged overpouch.

- The inner bag is made of a multilayer polymer film, alternatively Excel or Biofine
 - The Excel inner bag film consists of poly(propylene/ethylene)copolymer, thermoplastic elastomer (SEBS) and copolyester. The port system consists of poly(propylene/ethylene) copolymer and thermoplastic elastomer (SEBS). The infusion port is equipped with a polyolefin cap. The additive port is equipped with a synthetic polyisoprene (latex-free) stopper.
 - The Biofine inner bag film consists of poly(propylene/ethylene) copolymer and thermoplastic elastomers (SEBS and SIS). The infusion and additive ports are made of polypropylene and a thermoplastic elastomer (SEBS) equipped with synthetic polyisoprene stoppers.
- The oxygen absorber consists of iron powder in a polymer sachet.
- The integrity indicator (Oxalert™) consists of an oxygen sensitive solution in a polymer sachet.
- All packaging components are latex- and PVC-free.

Package sizes 1 x 250 ml, 10 x 250 ml
1 x 500 ml, 12 x 500 ml

Not all package sizes may be marketed.

6.6 Special precautions for disposal and other handling

The integrity indicator (Oxalert) should be inspected before removing the overpouch.

If the indicator is black, oxygen has penetrated the overpouch and the product should be discarded.

The overpouch, the oxygen absorber and the integrity indicator should be discarded after opening of the overpouch.

COMPATIBILITY

Additives

Only medicinal, nutritional or electrolyte solutions for which compatibility has been documented may be added to STRUCTOLIPID.

Additions should be made aseptically.

The normal daily requirement of water-soluble and fat-soluble vitamins, i.e. one bottle of SOLUVIT and one ampoule of VITALIPID ADULT, can be added to STRUCTOLIPID.

Before being added, SOLUVIT is reconstituted in either 10 ml of sterile water, STRUCTOLIPID or VITALIPID ADULT.

Mixing in plastic bag, (phthalate-free film)

The plastic bag used for admixing has to be sterile and be made of phthalate-free film.

Mixtures made up with STRUCTOLIPID should be prepared in a controlled and validated aseptic area.

STRUCTOLIPID can be mixed with the amino acid solutions GLAMIN, VAMIN 18 ELECTROLYTE FREE or INTRAFUSIN 15%, glucose solutions, trace elements in the form of

TRACEL, vitamins, i.e. SOLUVIT and VITALIPID ADULT, and electrolytes in the amounts indicated below.

TRACEL and electrolytes are added to the amino acid solution.

ADDIPHOS or any other inorganic phosphate source should be added to the glucose solution. The amino acid and glucose solutions with the additives are transferred to a plastic bag (phthalate-free film).

Vitamins, i.e. SOLUVIT and VITALIPID ADULT can be added to STRUCTOLIPID.

Finally, STRUCTOLIPID with additives is transferred to the plastic bag which is turned with caution until a homogeneous mixture is obtained.

The content of vitamin C in the mixture decreases due to oxidation. Vitamin C deficiency in prolonged intravenous nutrition including SOLUVIT, has not been reported, however.

Limits for mixture components.

Structolipid	250-750 ml
Glamin/Vamin 18 Electrolyte Free/ Intrafusin 15%	500-1000 ml
Glucose 10% /	1000 ml
Glucose 20% /	1000-1500 ml
Glucose 30% /	500-1000 ml
Glucose 40% /	500 ml
Glucose 50%	500*-750**ml
Tracel	0-10 ml
Vitalipid Adult	0-10 ml
Soluvit	0-1 bottle

Electrolyte limits in ready-mixed bags

mmol/1000 ml	
Sodium	0-150
Potassium	0-150
Calcium	1-5
Magnesium	0.5-5
Phosphate ***	0-15

* For stability reasons, 500 ml glucose 50% can only be mixed with 500-750 ml Structolipid when Glamin or Vamin 18 Electrolyte Free is used.

** For stability reasons, 750 ml glucose 50% can only be mixed with

1000 ml Glamin, Vamin 18 Electrolyte Free or Intrafusin 15%
500-750 ml Structolipid.

*** Includes the amount from Structolipid.

STABILITY

Without additives

After opening the container, the emulsion should be used directly due to the risk of microbiological contamination. The left-over contents of an opened bag should be discarded and not saved for later use.

Additives

When additions are made to STRUCTOLIPID, the infusion should be used directly after preparation due to the risk of microbiological contamination.

The left-over contents of an opened bag should be discarded and not saved for later use.

Mixing in plastic bag (phthalate-free film)

The physical in-use stability has been demonstrated for 72 hours in a refrigerator (2-8°C) followed by an infusion period of up to 24 hours. From a microbiological point of view, the product should be used immediately after supplementation. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and should normally not be longer than 24 h at 2-8°C unless additions have taken place in controlled and validated aseptic conditions.

If the admixtures have been stored after mixing a cream layer can be presented. Turn gently until a homogenous mixture is obtained before use.

7 MARKETING AUTHORISATION HOLDER

[To be completed nationally]

8 MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation:

Date of latest renewal:

[To be completed nationally]

10 DATE OF REVISION OF THE TEXT

2015-05-06