SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Omegaven®

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

100 ml emulsion contains:

Highly refined fish oil	10.0 g
containing	
eicosapentaenoic acid (EPA)	1.25 - 2.82 g
docosahexaenoic acid (DHA)	1.44 - 3.09 g
dl-α-Tocopherol (as antioxidant)	0.015 - 0.0296 g
Glycerol	2.5 g
Purified egg phosphatide	1.2 g

Total energy:	470 kJ/100 ml = 112 kcal/100 ml
pH value:	7.5 to 8.7
Titration acidity:	< 1 mmol HCl/l
Osmolality:	308-376 mosm/kg

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Emulsion for infusion
White homogenous emulsion

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Parenteral nutrition supplementation with long chain omega-3-fatty acids, especially eicosapentaenoic and docosahexaenoic acid, when oral or enteral nutrition is impossible, insufficient or contraindicated.

4.2 Posology and method of administration

Posology

Daily dose:
1 ml up to max. 2 ml Omegaven/kg body weight
= 0.1 g up to max. 0.2 g fish oil/kg body weight
= 70 ml up to max. 140 ml Omegaven for a patient with a body weight of 70 kg.

Maximum infusion rate:
The infusion rate should not exceed 0.5 ml Omegaven/kg body weight/hour corresponding to 0.05 g fish oil/kg body weight/hour.

The maximum infusion rate should be strictly adhered to, otherwise a severe increase in the serum triglyceride concentration can be observed.

Omegaven should be administered simultaneously with other fat emulsions. On the basis of a recommended total daily lipid intake of 1 - 2 g/kg body weight, the fish oil portion from Omegaven should constitute 10 - 20% of this intake.

Method of administration

- For infusion via central or peripheral vein.
- Containers should be shaken before use.
- When Omegaven is to be administered with other infusion solutions (eg amino acid solutions, cabohydrate solutions) via a common infusion line (by-pass, y-tube), the compatibility of the solutions/emulsions used must be ensured.

Duration of administration

The duration of administration should not exceed 4 weeks.

4.3 Contraindications

Severe haemorrhagic disorders.

Certain acute and life-threatening conditions such as:
- collapse and shock
- recent cardiac infarction
- stroke
- embolism
- undefined coma status

Due to lack of experience Omegaven should not be administered in patients with severe liver or renal insufficiency.
Omegaven should not be used in premature infants, newborns, infants and children due to limited experience.

General contra-indications for parenteral nutrition:
- hypokalaemia
- hyperhydration
- hypotonic dehydration
- unstable metabolism
- acidosis

Omegaven must not be administered to patients known to be allergic to fish or egg protein or to any of the active substances or excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Omegaven should be given with caution to patients with an impaired lipid metabolism and uncontrolled diabetes mellitus.

The serum triglyceride level should be monitored daily. Checks of blood glucose profiles, acid base metabolism, serum electrolytes, fluid balance, blood count and bleeding time in patients treated with anticoagulants must be carried out regularly. The serum triglyceride concentration should not exceed 3 mmol/l during the infusion of fat emulsions.

4.5 Interaction with other medicinal products and other forms of interaction

The infusion of Omegaven can cause a prolonged bleeding time and an inhibited platelet aggregation. Therefore, Omegaven should be administered with caution to patients requiring anticoagulant therapy even with regard to a possible reduction of anticoagulants.

4.6 Fertility, pregnancy and lactation

There is no evidence on the safety of this medicine during pregnancy or breastfeeding. This medicine should be used during pregnancy and breastfeeding only if strictly necessary.

4.7 Effects on ability to drive and use machines

Not applicable

4.8 Undesirable effects

Undesirable effects observed during the administration of Omegaven:

Investigations:
Rare (≥ 1/10,000, <1/1,000): The infusion of Omegaven can lead to a prolonged bleeding time and an inhibited platelet aggregation. Clinically relevant abnormalities have not been observed.

Gastrointestinal Disorders:
Rare (≥ 1/10,000, <1/1,000): fishy taste

Undesirable effects observed during the administration of fat emulsions:

	Uncommon *≥ 1/1,000 to <1/100*	*Rare* *≥ 1/10,000 to <1/1,000*	*Very rare* *< 1/10,000*
Blood and lymphatic system disorders			Thrombocytopenia, haemolysis, reticulocytosis
Gastrointestinal disorders	Abdominal pain nausea, vomiting		
General disorders and administration site conditions	Rise in body temperature, shivering, chills, tiredness		
Immune system disorders			Anaphylactic reaction
Investigations			Transient increase in liver function test
Metabolism and nutrition disorders	Hypertriglyceridaemia		
Nervous system disorders	Headache		
Reproductive system and breast disorders			Priapism
Skin and subcutaneous tissue disorders			Rash, urticaria
Vascular disorders			Circulatory effects (e.g. hyper/hypotension)

Trombocytopenia has been reported in association with prolonged treatment with fat emulsions in infants.
Transient increase in liver function tests after prolonged intravenous nutrition with or without fat emulsions have also been noted. The reasons are not clear at present.

Possible signs of metabolic overload must be observed. The cause may be genetic (individually different metabolisms) and with respect to different previous illnesses with varying rapidity and following different doses, but has been observed mainly with the use of cottonseed oil emulsions.

- Metabolic overload might give the following symptoms:
- hepatomegaly with or without icterus
- a change or reduction of some coagulation parameters (e.g. bleeding time, coagulation time, prothrombin time, platelet count)
- splenomegaly
- anaemia, leucopenia, thrombocytopenia
- bleedings and tendency to bleed
- pathological liver function tests
- fever
- hyperlipidaemia
- headache, stomach pains, fatigue
- hyperglycemia.

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

Reporting of suspected adverse reactions
Side effects can be reported to the Ministry of Health by clicking on the link “Report Side Effects of Drug Treatment” that appears on the homepage of the Ministry of Health’s website (www.health.gov.il) which links to an online form for reporting side effects, or by following this link: https://sideeffects.health.gov.il, and by emailing the Registration Holder's Patient Safety Unit at: drugsafety@neopharmgroup.com

4.9 Overdose

Overdose leading to fat overload syndrome may occur when the triglyceride level during lipid infusion rises above 3 mmol/l, acutely, as a result of too rapid infusion rate, or chronically at recommended rates of infusion in association with a change in the patient´s clinical condition e.g. renal function impairment or infection.

Overdosage may lead to side-effects (see 4.8).

In these cases, the lipid infusion should be stopped or, if necessary, continued at a reduced dosage. The administration of fat also has to be stopped if a marked increase in blood glucose levels occur during infusion of Omegaven. A severe overdosage of Omegaven without simultaneous administration of a carbohydrate solution, may lead to metabolic acidosis.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Emulsion for parenteral nutrition.
ATC-Code: B05BA02

The long-chain omega-3 fatty acids in Omegaven are partly incorporated in plasma and tissue lipids. Docosahexaenoic acid is an important structural element in membrane phospholipids, while

eicosapentaenoic acid is a precursor in the synthesis of a special class of eicosanoids (prostaglandins, thromboxanes, leukotrienes, and other lipid mediators). Increased synthesis of these eicosapentaenoic acid-derived mediator substances may help promote antiaggregatory, and anti-inflammatory effects, and is associated with immunomodulatory effects.

The glycerol contained in Omegaven is designed for use in energy production via glycolysis or is re-esterified together with free fatty acids in the liver to form triglycerides.

Omegaven also contains egg phospholipids, which are hydrolysed or incorporated into the cell membranes, where they are essential for the maintenance of membrane integrity.

5.2 Pharmacokinetic properties

The lipid particles infused with Omegaven are similar in size and elimination to physiological chylomicrons. In healthy male volunteers, a triglyceride half-life for Omegaven of 54 minutes has been calculated.

5.3 Preclinical safety data

Preclinical data reveal no special hazard for humans based on conventional studies of acute and repeated dose toxicity, safety pharmacology and genotoxicity. Animal studies to evaluate the *reproductive* toxicity have not been conducted.

Sensitisation tests

In a test in guinea pigs (Maximisation test) Omegaven showed moderate dermal sensitisation. A systemic antigenicity test gave no indication of evidence of anaphylactic potential of Omegaven.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium oleate, sodium hydroxide, water for injections

6.2 Incompatibilities

Incompatibilities may occur through the addition of polyvalent cations, e.g. calcium, especially when combined with heparin.

6.3 Shelf life

Shelf life of the medicinal product as packaged for sale:

The expiry date of the product is indicated on the packaging materials.

Shelf life after dilution or reconstitution according to directions:

Chemical and physical in-use stability of mixtures containing Omegaven has been demonstrated for 24 hours at 25 °C and data is available from the manufacturer. From a microbiological point of view, mixtures with fat emulsions or fat emulsions containing fat-soluble vitamins should be used immediately. If not used immediately, in-use storage time and conditions prior to use are the responsibility of the user. Only if compounding has taken place in controlled and validated aseptic conditions can storage conditions be based on the manufacturers stability data. From a microbiological point of view, mixtures compounded in uncontrolled and unvalidated conditions should normally be used within 24 hours, including the infusion time (see 6.6 for further information).

Shelf life after first opening the container:

Omegaven should be used with sterile transfer equipment immediately after opening.
To be used immediately after breaking the vial seal.

6.4 Special precautions for storage

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

6.5 Nature and contents of container

Packs containing 10 glass vials with 50 or 100 ml emulsion.
Glass bottles (type II, colourless). Halobutyl rubber stoppers.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

- Containers should be shaken before use.
- Use only if the emulsion is homogeneous and the container is undamaged.
- Non-phthalate containing equipment should be used for administration wherever possible.
- Any portions of contents as well as mixtures remaining after use should be discarded.

Omegaven may be aseptically mixed with fat emulsions as well as fat-soluble vitamins. When simultaneously administered with other fat emulsions admixed or diluted before administration (see 6.2 and 6.3.for further information), the fish oil portion from Omegaven should constitute 10-20% of the total daily lipid intake.

7 MANUFACTURER

Fresenius Kabi Deuctschland GmbH
Else-Kroner St.1, DE-61352, Bad Homburg, Germany

8 REGISTRATION HOLDER

Cure Medical & Technical Supply
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9 REGISTRATION NUMBER(S)

123-18-30247

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