

NEW ZEALAND DATA SHEET

1 PRODUCT MEDICINE

Omegaven, emulsion for infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Omegaven contains the following:

Content

Active Ingredients	g/100 mL
Fish oil - rich in Omega-3 acids containing:	10.0
Eicosapentaenoic acid (EPA)	1.25-2.82
Docosahexaenoic acid (DHA)	1.44-3.09
dl- α -tocopherol (as antioxidant)	0.015-0.0296
Glycerol	2.5
Egg lecithin	1.2
Total energy per 100 mL	470 kJ (112 kcal)
pH value	7.5 to 8.7
Titration acidity	< 1 mmol HCl/L
Osmolality	308-376 mOsm/kg water

For the full list of excipients, see Section 6.1 List of excipients.

3 PHARMACEUTICAL FORM

Emulsion for Infusion.

White homogenous emulsion.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For use as a fraction of the lipid emulsion component for total parenteral nutrition, providing supplements of long chain omega-3-fatty acids especially eicosapentanoic and docosahexanoic acid when oral or enteral nutrition is impossible, insufficient or contraindicated.

4.2 Dose and method of administration

Daily dose:

1 mL up to maximum of 2 mL Omegeven/kg body weight
= 0.1 g up to a maximum of 0.2 g fish oil/kg body weight.
= 70 mL up to 140 mL Omegeven for a patient with a body weight of 70 kg.

Maximum infusion rate:

The infusion rate should not exceed 0.5 mL Omegeven/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 bodyweight, the fish oil portion from Omegaven should constitute 10-20% of this intake.

Method of administration

For infusion via central or peripheral vein.

When Omegaven is to be administered with other infusion solutions e.g. amino acid solutions, carbohydrate 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 contraindications 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 actives 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.

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Use in the elderly

No data available.

Paediatric use

No data available.

Effects on laboratory tests

No data available.

4.5 Interaction with other medicines and other forms of interactions

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

Effects on fertility

No studies have been performed.

Use in pregnancy (Category B2)

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

Use in lactation

There is no evidence on the safety of this medicine during breastfeeding.

4.7 Effects on ability to drive and use machines

Omegaven is unlikely to produce an effect on the ability to drive or use machinery.

4.8 Undesirable effects

Undesirable effects observed during the administration of Omegaven:

Investigations:

Rare ($\geq 1/10,000$, $<1/1,000$): 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 ($\geq 1/10,000$, $<1/1,000$): fishy taste

Undesirable effects observed during the administration of fat emulsions:

	<i>Uncommon $\geq 1/1,000$ to $<1/100$</i>	<i>Rare $\geq 1/10,000$ to $<1/1,000$</i>	<i>Very rare $< 1/10,000$</i>
<i>Blood and lymphatic system disorders</i>			Thrombocytopenia, haemolysis, reticulocytosis
<i>Immune system disorders</i>			Anaphylactic reaction
<i>Metabolism and nutrition disorders</i>	Hypertriglyceridaemia		
<i>Nervous system disorders</i>	Headache		
<i>Vascular disorders</i>			Circulatory effects

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	<i>Uncommon</i> ≥ 1/1,000 to <1/100	<i>Rare</i> ≥ 1/10,000 to <1/1,000	<i>Very rare</i> < 1/10,000
			(e.g. hyper/hypotension)
<i>Skin and subcutaneous tissue disorders</i>			Rash, urticaria
<i>Gastrointestinal disorders</i>	Abdominal pain nausea, vomiting		
<i>Reproductive system and breast disorders</i>			Priapism
<i>General disorders and administration site conditions</i>	Rise in body temperature, shivering, chills, tiredness		
<i>Investigations</i>			Transient increase in liver function test

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 illness 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
- hyperglycaemia

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

Reporting suspected adverse effects

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions <https://nzphvc.otago.ac.nz/reporting/>

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 section 4.8).

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

For advice on the management of overdose, please contact the National Poisons Centre on 0800 POISON (0800 764 766).

5 PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Blood Substitutes and Perfusion Solutions, I.V. Solutions, Solutions for Parenteral Nutrition, Fat emulsions

ATC code: B05B A02

5.1 Pharmacodynamic properties

Mechanism of action

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 eicosapentanoic acid-derived mediator substances may help promote antiaggregatory, and anti-inflammatory effects, and is associated with immunomodulatory effects.

The glycerol contained in Omegaven is intended 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 lecithin, which are hydrolysed or incorporated into the cell membranes, where they are essential for the maintenance of membrane integrity.

Clinical trials

No data available.

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.

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Genotoxicity

No special hazard for humans based on conventional studies for genotoxicity.

Carcinogenicity

No studies have been performed.

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

Approved Shelf Life before mixing

18 months

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. 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 section 6.6 for further information).

Shelf life after first opening of 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

Store below 25°C. Do not freeze.

6.5 Nature and contents of container

Type II clear glass bottle with bromobutyl rubber stoppers.

Pack sizes*

50mL x 10 bottles

100mL x 10 bottles

*Not all pack sizes may be marketed.

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6.6 Special precautions for disposal and other handling

Containers should be shaken before use. Use only if the emulsion is homogenous 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 section 6.2 and 6.3), the fish oil portion from Omegaven should constitute 10-20% of the total daily lipid intake.

No special requirements for disposal. Any unused medicine or waste material should be disposed of in accordance with local requirements.

7 MEDICINE SCHEDULE

General Sale Medicine

8 SPONSOR

Fresenius Kabi New Zealand Limited
60 Pavilion Drive
Mangere, Auckland 2022
New Zealand
Freecall: 0800 144 892

9 DATE OF FIRST APPROVAL

02 November 2006

10 DATE OF REVISION OF THE TEXT

12 April 2019

Summary table of changes

Section Changed	Summary of new information
All	Reformat Data Sheet as per new Medsafe requirements