

How Physicians Can Obtain Omegaven

(Revised April 22, 2008)

Note: many of these steps will occur concurrently so the prescriber should start submitting and not wait for a response to proceed to the next step:

1. Obtain permission from FDA...email Brian Strongin and Elizabeth Ford at the FDA to alert them that a request for Omegaven is forthcoming. Send them your contact information (including phone number) and brief information on the patient. It is not necessary to fax or send them any forms at that time. They will contact you and email you the proper documents.

Their email addresses are: brian.strongin@fda.hhs.gov and Elizabeth.ford@fda.hhs.gov

We typically hear back via phone within 1-2 days.

2. Submit a copy of the protocol you plan to follow to your Investigational Review Board
3. Place an order for Omegaven with International Pharmacy in Hamburg, Germany. Fresenius won't ship small orders, using this pharmacy is much easier if only obtaining for 1 patient. I am sure there are other international pharmacies that could also do this but this is who we have dealt with in the past. We are not endorsing them, it just the process we have followed.

If you use International Pharmacy, however, they will NOT accept US credit cards. The preferred method of payment for them would be an international bank transfer or wire transfer to our bank account. They will submit the bank details by email directly to the customer. Checks are still a hassle as they might be lost, take weeks, or the conversion rate has totally changed in the meantime. Shipping is extra.

This is their link: <http://www.pharmacy-international.de>

Mrs.ELENA EKROT
Export Sales
Pharmacy International
Hamburg (Germany)
Phone : +49 40 241 241
Fax: +49 40 280 2518
Email: mail@pharmacy-international.de

Once you place the order, they will email you when it is stock. Then you must call a courier to deliver it or have Pharmacy International ship it at an additional charge. International Pharmacy has several shipping options available.

Any questions: Please contact:
Kathleen Gura
Kathleen.Gura@childrens.harvard.edu
617-355-2336

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Omegaven®

Beneficial for :

- Post-traumatic and post-surgical patients
- Patients experiencing early stages of sepsis/SIRS
- Patients at risk of hyperinflammatory processes
- Patients whose immune function is in need of support
- Patients with inflammatory bowel diseases (Crohn's disease, ulcerative colitis)

OMEGAVEN : Qualitative and Quantitative Composition 1 00 ml emulsion contains: 1 0.0 g Highly refined fish oil containing: eicosapentaenoic acid (EPA) 1 .25 - 2.82 g; docosahexaenoic acid (DMA) 1 .44 -3.09 g; myristic acid 0.1 - 0.6 g; palmitic acid 0.25 - 1 .0 g; palmitoleic acid 0.3 -0.9 g; stearic acid 0.05 - 0.2 g; oleic acid 0.6 - 1 .3 g; linoleic acid 0.1 -0.7g; linolenic acid =0.2g; octadecatetraenoic acid 0.05-0.4g; eicosaenoic acid 0.05-0.3g; arachidonic acid 0.1 -0.4g; docosaenoic acid =0.15g; docosapentaenoic acid 0. 1 5 - 0.45 g; dl-a-Tocopherol (as antioxidant) 0.015 -0.0296 g. Glycerol 2.5 g. Purified egg phosphatide 1 .2 g. Total energy: 470 kJ/1 00 ml = 11 2 kcal/100 ml. pH value: 7.5 to 8.7. Titration acidity: <1 mmol HCl/l. Osmolality: 308-376 mosm/kg. PHARMACEUTICAL FORM. Emulsion for infusion. 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. 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. 1 40 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 1 0 - 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 (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: Should not exceed 4 weeks. CONTRAINDICATIONS: impaired lipid metabolism, severe haemorrhagic disorders, unstable diabetes mellitus. 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, acidoses. Omegaven should not be administered to patients known to be allergic to fish or egg protein. SPECIAL WARNINGS AND PRECAUTIONS FOR USE 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. Interaction with other medicaments 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. Pregnancy and lactation: There is no evidence on the safety of this medicine during pregnancy or breastfeeding. This medicine should not be used during pregnancy and breastfeeding. Undesirable effects: The infusion of Omegaven can lead to a prolonged bleeding time and an inhibited platelet aggregation. In rare cases patients may experience a fishy taste. Undesirable effects observed during the administration of fat emulsions: slight rise in body temperature, heat sensation and/or cold sensations, chills, flush or cyanosis, lack of appetite, nausea, vomiting, dyspnoea, headache, pain in the chest, back and loins, bone-pain, priapism (in very rare cases), increase or decrease in blood pressure, anaphylactic reactions (e.g. erythema). 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, hyperlipidemia, 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. 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 "Undesirable Effects"). 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 occurs during infusion of Omegaven. A severe overdosage of Omegaven without simultaneous administration of a carbohydrate solution, may lead to metabolic acidosis. PHARMACOLOGICAL PROPERTIES. Pharmacodynamic properties: Pharmacotherapeutic group: Emulsion for parenteral nutrition ATC-Code: BO5BA. The long-chain omega-Sfatty acids in Omegaven are partly incorporated in plasma and tissue lipids. Docosahexanoic acid is an important structural element in membrane phospholipids, while eicosapentanoic 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 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 hydrolized or incorporated into the cell membranes, where they are essential for the maintenance of membrane integrity. PHARMOKINETIC 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. PRECLINICAL SAFETY DATA: Preclinical data reveal no special hazards for humans based on conventional studies of acute and repeated dose toxicity, safety pharmacology and genotoxicity. No fertility studies have been conducted. Sensitisation tests: In a test in Guinea pigs (Maximization test), Omegaven showed moderate dermal sensitisation. A systemic antigenicity test gave no indication of evidence of anaphylactic potential of Omegaven. PHARMACEUTICAL PARTICULARS List of excipients: Sodium oleate, sodium hydroxide, water for injections. Special precautions for storage: Do not store above 25 °C. Do not freeze. Nature and contents of container: Packs containing 1 0 glass vials with 50 or 1 00 ml emulsion. Glass

bottles (type II , colorless). Bromobutyl rubber stoppers. Instructions for use/handling: To be used immediately after breaking the vial seal. 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. DATE: August 1 999.

Reference:

1. Grimminger F et al., Parenterale Omega- 3-lipidbehandlung bei inflammatorischen systemerkrankungen. Med Welt 1993, 44: 207-21
2. Carpentier YA: unpublished data
3. Grimminger F et al. Influence of n-3 lipid supplementation on fatty acid profiles & lipid mediator generation in patients with severe ulcerative colitis. Eur J Clin invest 1993; 23: 706-15.
4. Schauder P, Schenk HD, Korff C: unpublished data
5. B. Matthies, D. Kunz, et al, Influence of nutrition enrich with omega-3 fatty acids on cytokine levels in patients with major surgery
6. Wigmore J et al., The effect of polyunsaturated fatty acids on progress of cachexia in patients with pancreatic cancer. Nutrition (1996) 12: 27-30.