Prescribing Information

Omacor

1. Name of the medicinal product

OMACOR®, 1000 mg, soft capsules

2. Qualitative and quantitative composition

One capsule contains

Omega-3-acid ethyl esters 90……1000mg

comprising 840 mg eicosapentaenoic acid (EPA) ethyl ester (460mg) and docosahexaenoic acid (DHA) ethyl ester (380mg), including also as antioxidant 4 mg d-alpha-tocopherol (mixed with a vegetable oil e.g. soya oil).

For a full list of excipients see section 6.1.

3. Pharmaceutical form

Capsule, soft.

Soft, oblong, transparent gelatin capsules containing pale yellow oil.

4. Clinical particulars

4.1 Therapeutic indications

Post Myocardial Infarction

Adjuvant treatment in secondary prevention after myocardial infarction, in addition to other standard therapy (e.g. statins, antiplatelet drugs, betablockers, ACE inhibitors).

Hypertriglyceridemia

Endogenous hypertriglyceridemia as a supplement to diet when dietary measures alone are insufficient to produce an adequate response.

- type IV hypertriglyceridemia
- type IIb/III in combination with statins, when control of triglycerides by statins is insufficient

4.2 Posology and method of administration

Post Myocardial Infarction:

One capsule daily.

Hypertriglyceridemia

Initial treatment two capsules daily. If adequate response is not obtained, the dose may be increased to four capsules daily.

The capsules may be taken with food to avoid gastrointestinal disturbances.
There is limited clinical data regarding the use of Omacor in elderly patients over 70 years of age and patients with renal impairment (see section 4.4).
There is no information regarding the use of Omacor in children and adolescents or in patients with hepatic impairment (see section 4.4).

4.3 Contraindications

Hypersensitivity to the active substance, to soya or to any of the excipients listed in section 6.1.
Omacor contains soya oil. If you are allergic to peanut or soya, do not use this medicinal product.

4.4 Special warnings and precautions for use

Omacor should be used with caution in patients with known sensitivity or allergy to fish.
In the absence of efficacy and safety data, use of this medication in children is not recommended.
Clinical data regarding the use of Omacor in elderly patients over 70 years of age are limited.
Because of the moderate increase in bleeding time (with the high dosage, i.e. 4 capsules), patients receiving anticoagulant therapy must be monitored and the dosage of anticoagulant adjusted if necessary (see section 4.5 Interaction with other Medicinal Products and other forms of Interaction). Use of this medication does not eliminate the need for the surveillance usually required for patients of this type.
Make allowance for the increased bleeding time in patients at high risk of haemorrhage (because of severe trauma, surgery, etc).
During treatment with Omacor, there is a fall in thromboxane A2 production. No significant effect has been observed on the other coagulation factors. Some studies with omega-3-acids demonstrated a prolongation of bleeding time, but the bleeding time reported in these studies has not exceeded normal limits and did not produce clinically significant bleeding episodes.
Only limited information regarding the use in patients with renal impairment is available.
In some patients a small but significant increase (within normal values) in ASAT and

ALAT was reported, but there are no data indicating an increased risk for patients with hepatic impairment. ALAT and ASAT levels should be monitored in patients with any signs of liver damage (in particular with the high dosage, i.e. 4 capsules).

Omacor is not indicated in exogenous hypertriglyceridaemia (type 1 hyperchylomicronaemia). There is only limited experience in secondary endogenous hypertriglyceridaemia (especially uncontrolled diabetes).

There is no experience regarding hypertriglyceridaemia in combination with fibrates.

4.5 Interaction with other medicinal products and other forms of interaction

Oral anticoagulants: See Section 4.4 Special warnings and precautions for use. Omacor has been given in conjunction with warfarin without haemorrhagic complications. However, the prothrombin time must be checked when Omacor is combined with warfarin or when treatment with Omacor is stopped.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no adequate data from the use of Omacor in pregnant women.

Studies in animals have not shown reproductive toxicity. The potential risk for humans is unknown and therefore Omacor should not be used during pregnancy unless clearly necessary.

Breastfeeding

There are no data on the excretion of Omacor in animal and human milk. Omacor should not be used during lactation.

Fertility

There are no adequate data on the effect of Omacor on fertility.

4.7 Effects on ability to drive and use machines

Effects on ability to drive and use machines have not been studied. Nevertheless, Omacor is expected to have no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

The frequencies of adverse reactions are ranked according to the following : very common (> 1/10), common (> 1/100 to < 1/10); uncommon (>1/1000 to < 1/100); rare (>1/10,000 to < 1/1000); very rare (< 1/10,000) ; not known

Immune system disorders:

Rare: hypersensitivity

Metabolism and nutrition disorders:

Uncommon: hyperglycaemia, gout

Nervous system disorders:

Uncommon: dizziness, dysgeusia, headache

Vascular disorders:

Uncommon: hypotension

Respiratory thoracic and mediastinal disorders:

Uncommon: epistaxis

Gastrointestinal disorders:

Common: gastrointestinal disorders (including abdominal distension, abdominal pain, constipation, diarrhoea, dyspepsia, flatulence, eructation, gastro-oesophageal reflux disease, nausea or vomiting)

Uncommon: gastrointestinal haemorrhage

Hepatobiliary disorders:

Rare: liver disorders (including transaminases increased, alanine aminotransferase increased and aspartate aminotransferase increased)

Skin and subcutaneous tissue disorders:

Uncommon: rash

Rare: urticariaNot known: pruritus

Reporting of suspected adverse reactions

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.

Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form.

https://sideeffects.health.gov.il/

4.9 Overdose

There are no special recommendations. Treatment should be symptomatic.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Omega-3-triglycerides including other esters and acids,

ATC code : C10AX06

The omega-3 series polyunsaturated fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are essential fatty acids.

Omacor is active on the plasma lipids by lowering triglyceride levels as a result of a fall in VLDL (very low density lipoprotein), and the substance is also active on haemostasis and blood pressure.

Omacor reduces the synthesis of triglycerides in the liver because EPA and DHA are poor substrates for the enzymes responsible for triglyceride synthesis and they inhibit esterification of other fatty acids.

The increase in peroxisomes of β-oxidation of fatty acids in the liver also contributes to the fall in triglycerides, by reducing the quantity of free fatty acids available for their synthesis. The inhibition of this synthesis lowers VLDL.

Omacor increases LDL-cholesterol in some patients with hypertriglyceridaemia. A rise in HDL-cholesterol is only small, significantly smaller than seen after administration of fibrates, and not consistent.

The long-term lipid-lowering effect (after more than one year) is not known. Otherwise there is no strong evidence that lowering triglycerides reduces the risk of ischaemic heart disease.

During treatment with Omacor, there is a fall in thromboxane A2 production and a slight increase in bleeding time. No significant effect has been observed on the other coagulation factors.

11,324 patients, with recent MI (< 3months) and receiving recommended preventive treatment associated with a Mediterranean diet, were randomised in the GISSI-Prevenzione study in order to receive Omacor (n=2,836), vitamin E (n=2,830), Omacor + vitamin E (n=2,830) or no treatment (n=2,828). GISSI-P was a multicentre, randomised, open-label study performed in Italy.

The results observed over 3.5 years, with Omacor 1g/day, have shown a significant reduction of a combined endpoint including all-cause death, non fatal MI and non fatal stroke (decrease in relative risk of 15 % [2-26] p=0.0226 in patients taking Omacor alone compared to control, and of 10 % [1-18] p=0.0482 in patients taking Omacor with or without vitamin E). A reduction of the second prespecified endpoint criteria including cardiovascular deaths, non fatal MI and non fatal stroke has been shown (decrease in relative risk of 20 % [5-32] p=0.0082 in patients taking Omacor alone compared to control, decrease in relative risk of 11 % [1-20] p=0.0526 in patients taking Omacor with or without vitamin E). The secondary analysis for each component of the primary endpoints has shown a significant reduction of all cause deaths and cardiovascular deaths, but no reduction of non fatal cardiovascular events or fatal and non fatal strokes.

5.2 Pharmacokinetic properties

During and after absorption, there are three main pathways for the metabolism of the omega-3 fatty acids:

- **the fatty acids are first transported to the liver where they are incorporated into** various categories of lipoproteins and then channelled to the peripheral lipid stores;
- the cell membrane phospholipids are replaced by lipoprotein phospholipids and the fatty acids can then act as precursors for various eicosanoids;
- the majority is oxidised to meet energy requirements.

The concentration of omega-3 fatty acids, EPA and DHA, in the plasma phospholipids corresponds to the EPA and DHA incorporated into the cell membranes.

Animal pharmacokinetic studies have shown that there is a complete hydrolysis of the ethyl ester accompanied by satisfactory absorption and incorporation of EPA and DHA into the plasma phospholipids and cholesterol esters.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction. In addition non-clinical literature data on safety pharmacology are indicating that there is no hazard for humans.

6. Pharmaceutical particulars

6.1 List of excipients

Capsule core:

Alpha-tocopherol, as an antioxidant

Capsule shell:

gelatin,

glycerol,

purified water,

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

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

Shelf life after first opening: 3 months.

6.4 Special precautions for storage

Store below 25 °C.

Do not freeze.

6.5 Nature and contents of container

White high density polyethylene (HDPE) bottle

1 x 100 capsules1 x 28 capsules

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Any unused product or waste material should be disposed of in accordance with local requirements.

Manufacturer:

Abbott Laboratories GmbH, Hannover, Germany

Registration Holder:

Abbott Medical Laboratories Ltd., Kiryat Atidim, POB 58099, Tel Aviv, 61580.

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