Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Omacor 1000 mg Soft Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsules contains Omega-3-acid ethyl esters 90-1000 mg comprising 840 mg eicosapentaenoic acid (EPA) ethyl ester (460mg) and docosahexaenoic acid (DHA) ethyl ester (380mg).

Excipient(s): may contain soya bean oil

For a full list of excipients, *see section 6.1*.

3 PHARMACEUTICAL FORM

Capsule, soft

Product imported from the UK
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 medicinal products, betablockers, ACE inhibitors).

Hypertriglyceridaemia

Endogenous hypertriglyceridaemia as a supplement to diet when dietary measures alone are insufficient to produce an adequate response:
- type IV in monotherapy,
- type IIb/III in combination with statins, when control of triglycerides is insufficient.

4.2 Posology and method of administration

Post Myocardial Infarction

One capsule daily.

Hypertriglyceridaemia

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 no information regarding the use of Omacor in children, in elderly patients over 70 years of age, or in patients with hepatic impairment *(see section 4.4),* and only limited information regarding the use in patients with renal impairment.

4.3 Contraindications

Hypersensitivity to the active substance, to soya or to any of the excipients

4.4 Special warnings and precautions for use

Warnings

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).

In the absence of efficacy and safety data, use of this medication in children is not recommended.

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.

Special precaution

Regular monitoring of hepatic function (ASAT and ALAT) is required in patients with hepatic impairment (in particular with the high dosage, i.e. 4 capsules).

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.

Lactation

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

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

The frequencies of adverse reactions are ranked according to the following : common (> 1/100, < 1/10); uncommon (>1/1000 < 1/100); rare (>1/10000, < 1/1000); very rare (< 1/10000), including isolated reports.

Infection and infestations
Uncommon: gastroenteritis

Immune system disorders:
Uncommon: hypersensitivity

Metabolism and nutrition disorders:
Rare: hyperglycaemia

Nervous system disorders:
Uncommon: dizziness, dysgeusia
Rare: headache

Vascular disorders:
Very rare: hypotension

Respiratory thoracic and mediastinal disorders:
Very rare: nasal dryness

Gastrointestinal disorders:
Common: dyspepsia, nausea
Uncommon: abdominal pain, gastrointestinal disorders, gastritis, abdominal pain upper
Rare: gastrointestinal pain,
Very rare: lower gastrointestinal haemorrhage

Hepatobiliary disorders:
Rare: hepatic disorders

Skin and subcutaneous tissue disorders:
Rare: acne, rash pruritic
Very rare: urticaria

General disorders and administration site conditions:
Rare: Ill-defined disorders

Investigations:
Very rare: white blood count increased, blood lactate dehydrogenase increased
Moderate elevation of transaminases has been reported in patients with hypertriglyceridaemia.

4.9 Overdose

There are no special recommendations.
Administer symptomatic treatment.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Other cholesterol and triglycerides reducers, 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.

11324 patients, with recent MI (<3 months) and receiving a recommended preventative treatment associated with a Mediterranean diet, were randomised in the GISSI-Prevenzione study in order to receive Omacor (n=2836), vitamin E (n=2830), Omacor + vitamin E (n=2830) or no treatment (n=2828). 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 pre-specified 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

No safety issues have been identified relevant to human use at the recommended daily intake.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule core
Alpha-tocopherol

Capsule shell
Gelatin
Glycerol
Purified water
Medium chain triglycerides
Lecithin (soya)

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

The shelf life expiry date for this product shall be the date shown on the container and outer package of the product on the market in the country of origin.

6.4 Special precautions for storage

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

6.5 Nature and contents of container

White (HDPE) bottle.
Packsize 1 x 28 capsules

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 PARALLEL PRODUCT AUTHORISATION HOLDER

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8 PARALLEL PRODUCT AUTHORISATION NUMBER

PPA 1562/32/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 29th of October 2010

10 DATE OF REVISION OF THE TEXT