

**IRISH MEDICINES BOARD ACT 1995, as amended**

**Medicinal Products (Control of Placing on the Market) Regulations, 2007, as amended**

**PPA1500/064/001**  
Case No: 2083758

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

**Profind Wholesale Ltd.**

**Unit 625, Kilshane Avenue, Northwest Business Park, Dublin 15, Ireland**

an authorisation, subject to the provisions of the said Regulations, in respect of the product

**Omacor 1000mg Soft Capsules**

the particulars of which are set out in the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **28/07/2010**.

Signed on behalf of the Irish Medicines Board this

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A person authorised in that behalf by the said Board.

## Part II

### Summary of Product Characteristics

#### 1 NAME OF THE MEDICINAL PRODUCT

Omacor 1000mg Soft Capsules

#### 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Omega-3-acid ethyl esters 90 1000mg

Comprising 840mg eicosapentaenoic acid (EPA) ethyl ester (460mg) and docosahexaenoic acid (DHA) ethyl ester (380mg).

For one capsule

Excipients: 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 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  $\beta$ -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 A<sub>2</sub> 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 of this product is the date shown on the bottle and outer carton of the product as marketed 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**

Cardboard carton containing an over-labelled white (HDPE) bottle.

Pack size: 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**

Profind Wholesale Ltd  
Unit 625, Kilshane Avenue  
Northwest Business Park  
Dublin 15  
Ireland

**8 PARALLEL PRODUCT AUTHORISATION NUMBER**

PPA1500/64/1

**9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorisation: 18th June 2010

**10 DATE OF REVISION OF THE TEXT**

July 2010