Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Omega-3-acid ethyl esters Lomegar 1000mg Capsules, Soft

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each soft capsule contains 1000mg of omega-3-acid-ethyl-esters 90, comprising 840 mg eicosapentaenoic acid (EPA) ethyl ester (460 mg) and docosahexaenoic acid (DHA) ethyl ester (380 mg).

Excipient with known effect: lecithin (soya).

For the 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 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 through statins alone is insufficient.

4.2 Posology and method of administration

Posology

Paediatric population

There are no data available regarding the use of omega-3-acid ethyl esters in children and adolescents.

Special populations

There are no data available regarding the use of omega-3-acid ethyl esters 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.

Method of administration

Adults and elderly below 70 years of age

Post Myocardial Infarction
One capsule daily

Hypertriglyceridemia
Initial treatment is 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.

4.3 Contraindications

Hypersensitivity to the active substances, to soya, peanut or to any of the other excipients listed in section 6.1.

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 per day), patients receiving anticoagulant therapy must be monitored and the dosage of anticoagulant adjusted if necessary (see section 4.5). 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).

Omega-3-acid ethyl esters Capsules are not indicated in exogenous hypertriglyceridaemia (type 1 hyperchylomicronaemia). There is only limited experience with omega-3-acid ethyl esters in secondary endogenous hypertriglyceridaemia (especially uncontrolled diabetes). There is no experience regarding the treatment of hypertriglyceridaemia in combination with fibrates.

Special precaution
Regular monitoring of hepatic function (aspartate aminotransferase - ASAT and alanine aminotransferase - ALAT) is required in patients with hepatic impairment (in particular with the high dosage, i.e. 4 capsules per day).

Paediatric population
In the absence of efficacy and safety data, omega-3-acid ethyl esters Capsules are not indicated for use in children or adolescents.

This medicinal product contains lecithin (soya). If the patient is allergic to peanut or soya, do not take this medicinal product (see section 4.3).

4.5 Interaction with other medicinal products and other forms of interaction

Oral anticoagulants: see section 4.4 Special warnings and precautions for use.

Omega-3-acid ethyl esters have been given in conjunction with warfarin without haemorrhagic complications. However, the prothrombin time must be checked when Omega-3-acid ethyl esters Capsules treatment is combined with warfarin or when treatment with Omega-3-acid ethyl esters Capsules is stopped.

4.6 Fertility, pregnancy and lactation

Pregnancy
There are no adequate data from the use of omega-3-acid ethyl esters in pregnant women.

Studies in animals have not shown reproductive toxicity. The potential risk for humans is unknown and therefore Omega-3-acid ethyl esters Capsules should not be used during pregnancy unless clearly necessary.

Breastfeeding
There are no data on the excretion of omega-3-acid ethyl esters in animal and human milk, therefore Omega-3-acid

ethyl esters Capsules should not be used during lactation.

Fertility
No data are available.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

The frequencies of adverse reactions to omega-3-acid ethyl esters treatment are ranked according to the following: common (≥ 1/100 to < 1/10); uncommon (≥1/1,000 to < 1/100); rare (≥1/10,000 to < 1/1,000); very rare (< 1/10,000), 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: urticarial

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.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued

monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the online reporting option (preferred method) accessible from the IMB homepage (www.imb.ie). A downloadable report form is also accessible from the IMB website, which may be completed manually and submitted to the IMB via 'freepost' (see details below). Alternatively, the traditional post-paid 'yellow card' option may also be used.

FREEPOST
Pharmacovigilance Section
Irish Medicines Board
Kevin O'Malley House
Earlsfort Centre
Earlsfort Terrace
Dublin 2
Tel: +353 1 6764971
Fax: +353 1 6762517
Website: www.imb.ie
e-mail: imbpharmacovigilance@imb.ie

4.9 Overdose

There are no special recommendations.

Administer symptomatic treatment.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: 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.

Mechanism of action
Omega-3-acid ethyl esters are 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.

Pharmacodynamic effects
Omega-3-acid ethyl esters reduce 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.

Omega-3-acid ethyl esters increase 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 omega-3-acid ethyl esters, 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.

Clinical efficacy and safety
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.
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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 channeled 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 in sunflower oil
Capsule shell: gelatin, glycerol, purified water, medium-chain triglycerides, lecithin (soya)

6.2 Incompatibilities

Not applicable

6.3 Shelf life

18 months

This medicine should be used within 100 days of opening the bottle.

6.4 Special precautions for storage

Store below 25ºC. Do not freeze.

Keep the bottle in the outer carton in order to protect from the light.

6.5 Nature and contents of container

White, high density polyethylene (HDPE) bottle, with a snap-on cap and integrated seal both made from polyethylene (PE).

The bottles are supplied in cartons containing 28 capsules or 100 capsules

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Trygg Pharma AS
Fjordalleen 16
PO Box 1423 Vika
0115 Olso
Norway

8 MARKETING AUTHORISATION NUMBER

PA1849/001/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 29th November 2013

10 DATE OF REVISION OF THE TEXT

June 2014