Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Trimega 1000 mg Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 1000 mg Omega-3-acid ethyl esters 90, comprising 840 mg eicosapentaenoic acid (EPA) ethyl ester (460 mg) and docosahexaenoic acid (DHA) ethyl ester (380mg).
Excipient with known effect: contains soya oil
For the full list of excipients see section 6.1.

3 PHARMACEUTICAL FORM

Capsule, soft.
Slightly yellow soft capsules, 23.8 mm x 9.5 mm

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

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

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

Method of administration
The capsules may be taken with food to avoid gastrointestinal disturbances.
There is limited clinical data regarding the use of Omega-3-acid ethyl esters 90 in elderly patients over 70 years of age and in patients with renal impairment (see section4.4).
There is no information regarding the use of Omega-3-acid ethyl esters 90 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.

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.

During treatment with Omega 3-acid-ethyl esters 90, 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.

Clinical data regarding the use of Omega 3-acid-ethyl esters 90 in elderly patients over 70 years of age are limited.

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).

Omega 3-acid-ethyl esters 90 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.

Systematic reviews and meta-analyses of randomized controlled clinical trials highlighted a dose-dependent increased risk of atrial fibrillation in patients with established cardiovascular diseases or cardiovascular risk factors treated with omega-3-acid ethyl esters compared to placebo. The observed risk is highest with a dose of 4 g/daily (see section 4.8). If atrial fibrillation develops, treatment should be permanently discontinued.

Trimega should be used with caution in patients with known sensitivity or allergy to fish.

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 90 have been given in conjunction with warfarin without haemorrhagic complications. However, the prothrombin time must be checked when Omega-3-acid ethyl esters 90 are combined with warfarin or when treatment with Omega-3-acid ethyl esters 90 are stopped.

4.6 Fertility, pregnancy and lactation

Pregnancy
There are no adequate data from the use of Omega-3-acid ethyl esters 90 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 90 should not be used during pregnancy unless clearly necessary.

Breastfeeding
There are no data on the excretion of Omega-3-acid ethyl esters 90 in animal and human milk. Omega-3-acid ethyl esters 90 should not be used during lactation.
Go to top of the page.

4.7 Effects on ability to drive and use machines

Effects on ability to drive and use machines have not been studied.
Nevertheless, Omega-3-acid ethyl esters 90 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: common (> 1/100, < 1/10); uncommon (>1/1000 < 1/100); rare (>1/10000, < 1/1000); very rare (<1/10000), Not known (cannot be estimated from the available data).

Immune system disorders:
Rare: hypersensitivity

Metabolism and nutrition disorders:
Uncommon: hyperglycaemia, gout

Nervous system disorders:
Uncommon: dizziness, dysgeusia, headache

Cardiac disorders:
Common: Atrial fibrillation

Vascular disorders:
Uncommon: hypotension

Respiratory thoracic and mediastinal disorders: Uncommon: epistaxis

Gastrointestinal disorders:
Common: gastrointestinal disorders (including abdominal distension, abdominal pain, constipation, diarrhea, 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: urticarial

Not known (cannot be estimated from the available data): Pruritus

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 HPRA Pharmacovigilance, Website: www.hpra.ie

4.9 Overdose

There are no special recommendations.
Treatment should be symptomatic.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Lipid modifying agents, 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.

Mechanism of action
Omega-3-acid ethyl esters 90 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.
Omega-3-acid ethyl esters 90 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.

Pharmacodynamic effects
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.

Omega-3-acid ethyl esters 90 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.

During treatment with Omega-3-acid ethyl esters 90, 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.

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 (may contain vegetable oil e.g. soya oil)

Capsule shell:
Gelatin
Glycerol
purified water
Medium-chain triglycerides
Lecithin (sunflower)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

4 years.
Trimega soft gelatin capsules should be used within 100 days of opening the bottle.

6.4 Special precautions for storage

Do not store above 25ºC. Do not freeze.
For storage conditions after first opening of the medicinal product, see section 6.3.

6.5 Nature and contents of container

White (HDPE) bottle
- 1 x 28 soft gelatin capsules
- 1 x 30 soft gelatin capsules
- 1 x 60 soft gelatin capsules
- 1 x 100 soft gelatin capsules
- 10 x 28 soft gelatin capsules

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Clonmel Healthcare Ltd
Waterford Road
Clonmel, Co. Tipperary
E91 D768
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0126/236/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 17th August 2012
Date of last renewal: 16th August 2017.

10 DATE OF REVISION OF THE TEXT

January 2025