SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Omega 3-acid-ethyl esters 1000mg soft capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One capsule contains 1000 mg Omega-3-Acid Ethyl Esters 90, comprising principally 840 mg ethylesters of eicosapentaenoic acid (EPA) (465 mg) and docosahexaenoic acid (DHA) (375 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 capsule containing pale yellow coloured oily liquid imprinted with '740'.

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, anti-platelet medicinal products, beta-blockers, 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,
- typeIIb/III in combination with statins, when control of triglycerides is insufficient.

4.2 Posology and method of administration

Adults

Post Myocardial Infarction

One capsule daily.

Hypertriglyceridaemia

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.

Special populations

There is limited clinical data regarding the use of Omega 3-acid-ethyl esters Strides 1000mg soft capsules in older people over 70 years of age and patients with renal impairment (see section 4.4).

There is no information regarding the use of Omega 3-acid-ethyl esters Strides 1000mg soft capsules in children and adolescents or in patients with hepatic impairment (see section 4.4).

4.3 Contraindications

Hypersensitivity to the active substance, to soya, peanut 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 per day), 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).

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).

Paediatric population

In the absence of efficacy and safety data, use of this medication in children and adolescents

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 older people 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 per day).

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 the treatment of 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.

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 is 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.

Breast-feeding

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.

Fertility

No data available

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: very common (≥ 1/10), common (≥ 1/100 to < 1/10); uncommon (≥1/1000 to < 1/100); rare (≥1/10000 to < 1/1,000); very rare (< 1/10,000).

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: urticaria

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 Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

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.

Mechanism of action

Omega-3-acid ethyl esters 90 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 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.

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. Otherwise there is no strong evidence that lowering triglycerides reduces the risk of ischaemic heart disease.

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.

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 Omega-3-acid ethyl esters 90 (n=2836), vitamin E (n=2830), Omega-3-acid ethyl esters 90 + 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 Omega-3-acid ethyl esters 90 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 Omega- 3-acid ethyl esters 90 alone compared to control, and of 10% [1-18] p=0.0482 in patients taking Omega-3-acid ethyl esters 90 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 Omega-3-acid ethyl esters 90 alone compared to control, decrease in relative risk of 11% [1- 20] p= 0.0526 in patients taking Omega-3-acid ethyl esters 90 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 are 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 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

Capsule shell:

Gelatin Glycerol purified

water

Medium-chain triglycerides Isopropyl

alcohol

Opacode white printing ink

(Composition of Opacode white ink is Shellac glaze, Titanium dioxide, Purified water, N-butyl alcohol, Lecithin (soya), Simeticone)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

Shelf life after first opening of HDPE container is 120 days.

6.4 Special precautions for storage

Store below 30°C.

Keep the container in the outer carton in order to protect from the light. For shelf life after first opening of HDPE please refer section 6.3.

6.5 Nature and contents of container

White opaque HDPE container with white opaque HDPE screw closure with induction sealing. Each bottle contains 20, 28, 100 and 120 capsules.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

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

7 MARKETING AUTHORISATION HOLDER

Strides Pharma UK Limited,

Unit 4, Metro Centre, Tolpits Lane, Watford,

Hertfordshire WD 189 SS United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 13606/0223

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

15/07/2014

10 DATE OF REVISION OF THE TEXT

15/01/2019