Summary of Product Characteristics

1. NAME OF THE MEDICINAL PRODUCT (FPP)

FORTALINE® PLUS
Omega 3 fatty acids – vitamin E

1.1 Strength 500 mg (18% EPA-12% DHA) - 10 mg
1.2 Pharmaceutical form : soft capsule

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule of Fortaline Plus contains 500 mg of marine lipid concentrate (fish oil) with minimum 30 % of essential omega 3 fatty acids (standardised to 18% EPA and 12% DHA) and 10 mg of vitamin E (α-tocopherylacetate).

For the full list of excipients: see section 6.1

3. PHARMACEUTICAL FORM

Soft capsule
Clear, oval shaped, capsule containing a clear oily liquid.
The capsules are manufactured via EnteriCare™ Anti-Reflux Technology.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

As essential nutrient Fortaline Plus is indicated to restore the balance between the Omega-6 and the Omega-3 fatty acids.
The most beneficial and most active of these fatty acids are EPA (eicosapentaenoic acid) and DHA (docosahexaenoic acid), which play a crucial role in the prevention of arteriosclerosis, heart attack, depression and cancer.
An adequate intake of both fatty acids during pregnancy and lactation improves the healthiness of mother, foetus and the new born.

Omega 3 fatty acids are beneficial to everybody, and a daily intake is recommended to improve health and development. Docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) are essential fatty acids which are important for a proper development associated with :

- Increase in birth weight and decrease in the risk of premature birth.
- Improvement of brain development, and of visual development.
- Protection of the skin from aging.
- Support of the immune system.
- Support of heart and blood pressure
- Improvement of the metabolism.
- Increase in flexibility of the joints.
- Improvement of emotional well-being and positive mental outlook; decrease of stress.

4.2. Posology and mode of administration

4.2.1. Posology

Adults

Oral use, one or two capsules per day

4.2.2. Special populations

Pregnant and lactating women

Oral use, two to three capsules per day

4.2.3. Paediatric population

Children which are able to swallow a capsule

Oral use, one capsule per day

4.2.4. Method of administration

Swallow the capsule with a glass of water**.**

The EnteriCare™ technology reduces the risk of reflux and enables to avoid a fishy aftertaste.

It is essential for patients to know that these capsules should not be used to replace a balanced diet.

4.3. Contraindications

- History of hypersensitivity to any of the ingredients (see section 6).
- The use of aspirin and anti-coagulants such as warfarin is contra-indicated, because omega-3 fatty acids have an influence on the functioning of the blood platelets.
- Patients at high risk of bleeding.

4.4. Special warning and precautions for use

Patients should be informed to know that these capsules should not be used to replace a balanced diet.

Since fish oils are derived from marine life, allergic reactions are possible. Use of the product has to be interrupted if rash or other allergic reactions are observed. Patients should be advised to consult a doctor immediately.

Before undergoing elective surgery, use of this supplement has to be interrupted before the procedure. The surgeon should be alerted of the use of taking fish oil prior to scheduling the surgery.

Disorders of liver and kidneys
Studies have shown that the dietary supplementation with fish oil improves the renal function of normal subjects, as well as that of patients with renal failure of different aetiologies.
Administration of fish oil for 1 month was unable to improve renal function in cirrhotic patients with ascites and renal failure. The occurrence of undesirable effects, such as the reduction of arterial pressure and the prolongation of bleeding time, argues against the use of fish oils in these patients.

4.5. Interactions with other medicinal products and other forms of interactions

Some studies reported that some important bleeding occurred when fish oil was combined with aspirin or warfarin.

4.6. Fertility, pregnancy and lactation

4.6.1. Fertility

Animal studies support the role of omega-3 fatty acids in the reproduction mechanism.

4.6.2. Pregnancy

EPA and DHA fatty acids are administrated as supplement in the diet for pregnant women. They have a positive influence on the development of the foetus during the last three months of the pregnancy.

4.6.3. Lactation

EPA and DHA fatty acids are administrated as supplement in the diet for lactating women. Fortaline Plus has a positive influence on the new born during the lactating period.

4.7. Effects on the ability to drive and use machines

Fortaline Plus does not affect the ability to drive or use any tools or machines.

4.8. Undesirable effects

The following serious adverse reactions require the attention of a doctor or healthcare professional:

- mood changes or emotions,
- easy bruising,
- rash, or unusual skin reactions.

Most common undesirable effects are gastrointestinal disorders, such as nausea or dyspepsia.

Uncommon, rare to very rare undesirable effects:

- bad breath (fish breath),
- belching,
- diarrhoea,
- heartburn,
- stomach upset,
- weight gain.

None of the serious adverse events, reported in various trials of omega-3 fatty acid consumption, were associated with events such as death, life-threatening illness, or significant disability or handicap.
Two studies reported that some important bleeding occurred with fish oil combined with aspirin or warfarin.

4.9. Overdose

No cases of overdose have been reported.
In case of overdose, there are no particular recommendations. Symptomatic treatment must be put in place.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group and ATC code:
C10AX06: Other lipid modifying agents: Omega-3-triglycerides including other esters and acids.
A11HA03: Other plain vitamins: Tocopherol (Vitamin E)

The omega-3 polyunsaturated fatty acids , eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are essential fatty acids.
The exact mechanism of action of omega-3-carboxylic acids is unknown. However, possible mechanisms include: increased liver mitochondrial beta-oxidation, increased plasma lipoprotein lipase activity, inhibition of acyl-CoA: 1, 2-diacylglycerol acyltransferase, and decreased liver lipogenesis.
Furthermore, omega-3-carboxylic acids may decrease the production of liver triglycerides because they are poor substrates for the enzymes that participate in triglyceride synthesis, and they inhibit esterification of other fatty acids.

Vitamin E appears to act as an anti-oxidant within membranes, preventing propagated oxidation of unsaturated fatty acids.

5.2. Pharmacokinetic properties

Absorption

Following oral administration, polyunsaturated fatty acids (PUFAs) are absorbed normally as food substances at the normal food rate. EPA takes 5 to 8 hours to achieve peak concentration . DHA takes 5 to 9 hours to achieve peak concentration.

Distribution

Eicosanoids are localised tissue hormones. They do not travel in the blood, but are created in the cells. EPA and DHA are mainly bound to phospholipids.

Vitamin E enters the blood via the chylomicrons in the lymph and is bound to beta-lipoproteins. It is widely distributed to all tissues, and stored in adipose tissue.

Metabolism

The liver is the primary metabolism site. EPA and DHA are primarily oxidised in the liver similar to fatty acids derived from the diet.

Some vitamin E is metabolised in the liver to glucuronides of tocopheronic acid and its γ-lactone.

Omega-3 and omega-6 fatty acids share the same pools of enzymes and go through the same oxidation pathways while being metabolised. Once ingested, alanine (ALA) and linolenic acid (LA) can be elongated and desaturated into Long chain (LC) PUFAs. LA is converted into gamma-linolenic acid (GLA, 18:3 n-6), an omega-6 fatty acid that is a positional isomer of ALA. GLA, in turn, can be converted to the long-chain omega-6 fatty acid, arachidonic acid (AA, 20:4 n-6). ALA can be converted, to a lesser extent, to the long-chain omega-3 fatty acids, eicosapentaenoic acid (EPA; 20:5 n-3) and docosahexaenoic acid (DHA; 22:6n-3). However, the conversion from parent fatty acids into LC PUFAs occurs slowly in humans, and conversion rates are not well understood.

Elimination

After beta-oxidation the unsaturated fatty acids are following the elimination pathway of normal food substances.

Omega-3-carboxylic acids are not excreted via the kidneys. The total body clearance of EPA is 548 ml/h ; the total body clearance of DHA is 518 ml/h and.

The elimination half-life of EPA is 37 hours ; the elimination half-life of DHA is 46 hours.

Some vitamin E is excreted in the urine, but most of a dose is slowly excreted in the bile.

5.3. Preclinical safety data

General toxicity
Three times the maximum safe daily dosage only shows an increase in cholesterol and HDL and no interference with other function.
Acutely and chronically, there were no differences in external appearance, level of activity, daily food consumption, blood cell count, kidney function, thyroid function, prothrombin time (PT), and activated partial prothrombin time (PTT), which remained within normal ranges.

Reproductive toxicity
Results of a recent study indicated that supplementing bull semen extender with n-3 fatty acid and α-tocopherol improved post-thawed in vitro characteristics of Brown Swiss bull sperm.
In humans, clinical studies showed that dietary omega-3 supplementation increased sperm concentration, motility, and morphology, and also antioxidant activity in human seminal fluid.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

- Gelatin
- Glycerol
- Pectin
- Calcium chloride dihydrate
- Purified water

6.2. Incompatibilities

Co-administration with acetylsalicylic acid or anticoagulants (see section 4.3)

6.3. Shelf life

36 months.

6.4. Special precautions for storage

Store below 30°C, in the original packaging to protect from light and humidity.

6.5. Nature and contents of container

PVC-PVdC/Aluminium blister with 10 capsules.
Box with 20 capsules (2 blisters).

6.6. Special precautions for disposal and other handlings

No special requirements.
Any unused product or waste material should be disposed of in accordance with the local requirements.

7. MARKETING AUTHORISATION HOLDER AND MANUFACURING SITE ADDRESS

7.1. Marketing Authorization Holder

Dafra Pharma GmbH, Mühlenberg 7, 4052 Basel, Switzerland.

7.2. Manufacturer

Capsules: Patheon Softgels b.v., De Posthoornstraat 7, 5048 AS Tilburg, The Netherlands.
Packaging: Tjoapack Netherlands b.v., Nieuwe Donk 9, 4879 AC Etten-Leur, The Netherlands.

8. MARKETING AUHORISATION NUMBER

See list of MAs per country

9. DATE OF FIRST REGISTRATION

See list of MAs per country

10. DATE OF REVISION OF TEXT

January 2020.