

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Essentiale Capsule 300 mg

Hard capsule

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Drug substance:

1 hard capsule contains:

300 mg de-oiled enriched Phospholipids from soya beans. The phospholipids are quantified to 73 - 79 % Phosphatidylcholin, contains up to 7 % Phosphatidylethanolamin and less than 0.5 % Phosphatidylinositol.

Contains soy oil. For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Hard capsule for oral use.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Essentiale Capsule 300 mg is a herbal medicinal product for liver diseases.

Essentiale Capsule 300 mg is used to improve subjective symptoms, such as loss of appetite or a feeling of pressure in the upper right abdomen, in patients with liver damage caused by the toxic effects of certain foods or hepatitis.

4.2 Posology and method of administration

Posology

Age (body weight)	Single dose	Maximum daily dose
Adolescents (about 43 kg) and adults	2 Hard capsule (600 mg phospholipids from soya beans)	2 hard capsule 3 times daily (1800 mg of soybean phospholipids)

Children

The use in children under 12 years is not intended.

Essentiale Capsule 300 mg should be taken unchewed with sufficient liquid (preferably a [200 ml] glass of water) during meals.

In principle, there is no time limit for the duration of administration.

In the package leaflet, the patient is advised to take into account the information under precautions.

4.3 Contraindications

Hypersensitivity to the active substance, soybean proteins, peanut or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

In rare cases, this medicinal product can cause severe allergic reactions as it contains soya oil.

The patient is advised in the package leaflet that "This medicinal treatment is not a substitute for avoiding sources that damage the liver (e.g. alcohol)".

If you have chronic hepatitis, supportive treatment with soya bean phospholipids is only justified if an improvement in the subjective signs of your condition is observed under treatment. If the symptoms get worse or if other unclear symptoms appear, the patient should consult a doctor.

Children

Sufficient studies are not available concerning use of Essentiale Capsule 300 mg in children. Therefore, it should not be applied in children under 12 years of age.

4.5 Interaction with other medicinal products and other forms of interaction

An interaction between Essentiale Capsule 300 mg and anticoagulants cannot be ruled out. Therefore, it may be necessary to adjust the dose of this medicinal product.

The package leaflet contains an advice that patients should inform their doctor if they use Essentiale Capsule 300 mg at the same time as this type of medicine.

4.6 Pregnancy and lactation

Pregnancy

There are only limited amount of data from the use of Essentiale Capsule 300 mg during pregnancy. Animal studies concerning reproduction toxicity are insufficient (see section 5.3). The use of Essentiale Capsule 300 mg in pregnant women is not recommended.

Breastfeeding

It is not known whether components of soybean phospholipids or their metabolites pass into breast milk. A risk for breast-fed infants cannot be ruled out. Essentiale Capsule 300 mg should not be taken by breast-feeding women.

Fertility

Preclinical studies in animals have not demonstrated an effect on male or female fertility.

4.7 Effects on ability to drive and use machines

Essentiale Capsule 300 mg has no influence on the ability to drive and use machines.

4.8 Undesirable effects

The frequency of side effects is based on the following categories:

Very common ($\geq 1/10$)

Common (≥ 100 to $< 1/10$)

Uncommon ($\geq 1/1.000$ to $< 1/100$)

Rare ($\geq 1/10.000$ to $< 1/1.000$)

Very rare ($< 1/10.000$)

Not known (frequency cannot be estimated from the available data)

Investigations

Not known: Increased blood pressure

Cardiac disorders

Not known: Palpitations

Nervous system disorders

Not known: Dizziness

Gastrointestinal disorders

Not known: gastrointestinal disorders in the form of nausea, vomiting, soft stools and/or diarrhoea.

Skin and subcutaneous tissue disorders

Not known: allergic reactions such as exanthema and urticaria, pruritus.

Side effects that are not mentioned in the package leaflet should be reported to a doctor or pharmacist.

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 to Bundesinstitut für Arzneimittel und Medizinprodukte, Abt. Pharmakovigilanz, Kurt-Georg-Kiesinger Allee 3, D-53175 Bonn, Website: www.bfarm.de.

4.9 Overdose

There are no known cases of overdose or intoxication with Essentiale Capsule 300 mg. In the package leaflet, the patient is advised of the following: "It is possible that the side effects listed below could occur with greater intensity. In this case, please inform a doctor. He or she can decide whether any measures need to be taken."

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Liver therapy

ATC-Code: A05BA10

In many experimental models of acute liver damage, such as damage from ethanol, alkyl alcohol, tetrachloromethane, paracetamol and galactosamine, liver protective effects have been reported among the pharmacodynamic properties of the substance. In addition, inhibition of steatosis and fibrosis has also been observed in chronic models (ethanol, thioacetamide, organic solvents). The mechanism of action is assumed to be accelerated regeneration and stabilization of membranes, and inhibition of lipid peroxidation and collagen synthesis. There are no specific studies available on pharmacodynamics in man.

5.2 Pharmacokinetic properties

Animal experiments on pharmacokinetics have shown that orally administered radiolabeled soybean phospholipids were over 90% absorbed in the small intestine.

Most of the phospholipids were cleaved by phospholipase A into 1-acyl-lysophosphatidylcholine, approximately 50% of which was reacylated immediately into polyunsaturated phosphatidylcholine during the absorption process in the mucosa of the small intestine. The phosphatidylcholine reaches the blood through the lymph pathway and then passes into the liver in particular, mostly bound to HDL.

Pharmacokinetic studies in man were conducted with ^3H and ^{14}C radiolabeled dilinoleoylphosphatidylcholine, among other substances. The choline residue was labeled with ^3H and the linoleic acid with ^{14}C .

Peak ^3H concentrations were reached between 6 and 24 hours and accounted for 19.9% of the dose. The half-life of the choline component was 66 hours.

Peak ^{14}C concentrations were reached between 4 and 12 hours and were 27.9% of the dose. The half-life of this component was 32 hours. 2% of the ^3H and 4.5% of the ^{14}C markers were recovered in the feces. 6% of the ^3H and only trace amounts of the ^{14}C markers were recovered in the urine. These results therefore show that more than 90% of both isotopes were absorbed in the intestine.

5.3 Preclinical safety data

For soybeans phospholipids no studies on the toxicity after repeated administration are available. In toxicological studies, phosphatidylcholine (a constituent of phospholipids from soybeans) was orally administered to dogs (6 weeks) and rats (48 weeks). The NOAEL was 1000 mg / kg body weight (KG) in the dog study and 3750 mg / kg body weight in the rat study, which both corresponds approximately to 20 times the human equivalence dose.

With phospholipids from soybeans, doses up to 3750 mg / kg body weight did not affect fertility in rats (corresponds to 17 times the human equivalence dose).

Up to a dose of 1000 mg / kg (rats) and 500 mg / kg (rabbits), no teratogenic findings could be obtained in further studies. This corresponds to 4.5 times the human equivalence dose. However, since the studies carried out do not meet current requirements and are not complete, no final assessment of the findings on embryotoxicity can be made. Phosphatidylcholine (a component of phospholipids from soybeans) showed no teratogenic and embryotoxic effects in therapeutic doses in animal experiments. The lowest teratogen-embryotoxic daily dose after oral

administration is more than 1000 mg / kg body weight in rats and more than 500 mg / kg body weight in rabbits (equivalent to a 5.6 times human equivalence dose).

No mutagenic potential could be found in various older studies (in vitro). There are no studies on carcinogenicity.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Ethanol 96%, hard fat, soya oil (Ph.Eur.), hydrogenated castor oil, ethylvanillin, 1-(4-methoxyphenyl) ethanone, all-rac- α -tocopherol, gelatin, dyes E 171, E 172, , sodium lauryl sulfate, purified water.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Do not store above 25°C. Store in the original package in order to protect from moisture.

Do not use this medicine after the expiry date.

6.5 Nature and contents of container

30 hard capsules

50 hard capsules

100 hard capsules

250 hard capsules

600 (20x30) hard capsules (clinic pack)

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

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Brüningstraße 50
65929 Frankfurt am Main

Tel.: 0800 56 56 010

Fax: 0800 56 56 011

E-Mail: medinfo-chc.de@sanofi.com

8. MARKETING AUTHORISATION NUMBER(S)

6385537.00.00

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

15.08.2003

10. DATE OF REVISION OF THE TEXT

April 2023

11. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product not subject to medical prescription.