Phospholipids
Essentiale® Forte P
300mg Hard Gel Capsule

Hepatoprotector
1. Name of the medicinal product
   Hard gel capsule
2. Qualitative and quantitative composition
   Pharmacologically active ingredient:
   1 capsule contains:
   De-oiled and enriched phospholipids from soya-beans 300 mg
   For the list of excipients see section 6.1.
3. Pharmaceutical form
   Hard gel capsule for oral use
4. Clinical particulars
4.1 Therapeutic indications
   Nutritional Support in the management of damaged liver (due to chronic liver disease, liver cirrhosis, fatty liver & intoxication by hepatotoxic substances).
4.2 Posology and method of administration

<table>
<thead>
<tr>
<th>Age and/or body weight</th>
<th>Single dose</th>
<th>Total daily dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children from 12 years (approx. 43 kg)</td>
<td>2 hard capsules (600 mg of soya-bean phospholipids)</td>
<td>3 times daily 2 hard capsules (1800 mg of soya-bean phospholipids)</td>
</tr>
<tr>
<td>Adolescents and adults</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Phospholipids (Essentiale Forte P) 300 mg hard gel capsule is taken unchewed with meals with plenty of liquid (e.g., with a glass of water).
Basically, the duration of the application is not limited.
The patient leaflet mentions that the information given under "precautions and warnings" should be taken into account.

4.3 Contraindications
Known hypersensitivity to soya-bean preparations or to any of the excipients.

4.4 Special warnings and precautions for use
   The leaflet draws the attention of the patient to the following:
   This drug therapy is not a substitute for the avoidance of the noxious agent causing liver damage (e.g., alcohol).
   In chronic hepatitis the adjuvant therapy with soya-bean phospholipids is justified only when improved subjective well-being becomes manifest during therapy.
   Consult your doctor when complaints aggravate or when other unclear complaints occur.
   Children
   As information about the administration in children is insufficient, phospholipids (Essentiale Forte P) 300 mg hard gel capsule should not be given to children under 12 years of age.
   Due to the content in soya-bean oil the medicinal product may provoke severe allergic reactions.

4.5 Interaction with other medicinal products and other forms of interaction
   An interaction of Phospholipids (Essentiale Forte P) 300 mg hard gel capsule with anticoagulants cannot be excluded. For this reason, dose adjustment of the anticoagulant might be necessary.
   The leaflet advises the patient to consult a doctor in the case of simultaneous application.

4.6 Pregnancy and lactation
   Preparations from soya-beans are largely used in human food and so far no clue has appeared that would suggest any risk during pregnancy. Results from investigation are insufficient. For this reason, the use of phospholipids (Essentiale Forte P) 300 mg hard gel capsule is not recommended during pregnancy and lactation.

4.7 Effects on ability to drive and use machines
   Phospholipids (Essentiale Forte P) 300 mg hard gel capsule has no effect on the ability to drive and to use machines.

4.8 Undesirable effects
   For the evaluation of any adverse effects the following incidences are considered:
   very frequent (≥ 1/10)
   frequent (≥ 1/100 to < 1/10)
   occasional (≥ 1/1000 to < 1/100)
   rare (≥ 1/10,000 to < 1/1000)
   very rare (< 1/10,000)
   Occasionally the administration of Phospholipids (Essentiale Forte P) 300 mg hard gel capsule may provoke
gastrointestinal disorders, such as stomach complaints, soft stool and diarrhoea.
On very rare occasions allergic reactions may occur, such as exanthema and urticaria. The doctor or pharmacist should be informed about any undesirable effect not listed in the leaflet. The leaflet informs that the administration of Phospholipids (Essentiale Forte P) 300 mg hard gel capsule should be discontinued in the event of one of the above mentioned undesirable effects, especially in hypersensitivity reactions. The patient should consult the doctor who may decide about the severity and any measures that might be necessary.

4.9 Overdose
No overdose reaction nor symptom of intoxication has been reported to date with Phospholipids (Essentiale Forte P) 300 mg hard gel capsule.
The leaflet informs that the listed undesirable effects may be reinforced.
The patient should consult the doctor who may decide about the severity and any measures that might be necessary.

5. Pharmacological properties
5.1 Pharmacodynamic properties
ATC Code: A03DA
Among the pharmacodynamic properties reported were hepatoprotective effects found in numerous experimental models in acute liver damage (induced by ethanol, acetyl alcohol, carbon tetrachloride, paracetamol and galactosamine). Furthermore, it was also seen to inhibit steatosis and fibrosis in chronic liver damage models (induced by ethanol, thioacetamide, and organic solvents). Its suggested principal actions have been through accelerated membrane regeneration and stabilization, inhibited lipid peroxidation and inhibited collagen synthesis.

5.2 Pharmacokinetic properties
Animal experiments into the pharmacokinetics showed that more than 90% of the orally applied soya-bean phospholipids are absorbed in the small intestine. Most of it is split by phospholipase A to 1-alpha-
lysophosphatidylcholine, 50% of which is reacylated immediately into polyunsaturated phosphatidylcholine still during the process of absorption in the intestinal mucosa. This polyunsaturated phosphatidylcholine reaches the blood via the lymph pathway and from there mainly bound to HDL - it passes in particular to the liver.
Tests into human pharmacokinetics were performed with radioactively labeled dilinoleoyl-
phosphatidylcholine (1H and 14C). The choline moiety was 1H-labeled and the linoleic acid had the 14C-label.
The maximum 1H concentration was achieved after 6 to 24 hours and amounted to 19.9% of the dose.
The half-life for the choline component was 66 hours.
The maximum 14C concentration was achieved after 4 to 12 hours and amounted to 27.9% of the dose. The half-life for this component was 32 hours.
In the faeces were found 2% of the 1H and 4.5% of the 14C label, in the urine 6% of the 1H and only minor amounts of the 14C label.
These results show that both isotopes are absorbed to over 90% in the intestine.

6. Pharmaceutical particulars
6.1 List of excipients
Ethanol 96%, hard fat, soya-bean oil (Ph. Eur.), hydrogenated castor oil, ethyl vanillin,
1,4-methoxyphenyl)ethanone, alphacophosphol, gelatin, colouring agents E 171, 172, sodium laurylsulfate, purified water.

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
2 Years.

6.4 Special precautions for storage
Store in the original container, not above 25°C.
Store in the original container in order to protect from humidity.
Do not use after the expiry date.

6.5 Nature and contents of container
50 hard gel capsules in clear glass bottle

6.6 Special precautions for disposal
No special requirements.

Manufactured By:
A. Nattermann & Co GmbH
Nattermannallee 1,
D-50829 Cologne, Germany

Imported By:
sanofi-aventis Philippines Inc.
3/F Feliza Bldg., 108 V.A. Rufino St.
Legazpi Village, 1229 Makati City
Philippines

Date of the information
30 June 2007