Amendment date: 12 April 2019

1.3.1.1 Package Insert (clean)

SCHEDULING STATUS

S3

PROPRIETARY NAME AND DOSAGE FORM

Legalon® forte capsules

COMPOSITION

Each capsule contains:

173,0 mg – 186,7 mg of dried extract of milk thistle fruits corresponding to 140 mg of silymarin, calculated as silibinin.

List of excipients:

Polysorbate 80, povidone, mannitol, sodium carboxymethyl starch, magnesium stearate, iron oxides E172, titanium dioxide E171, gelatine, sodium lauryl sulphate.

PHARMACOLOGICAL CLASSIFICATION

A 7.4 Lipotropic agents

PHARMACOLOGICAL ACTION

Pharmacodynamic properties

Silymarin has a membrane-stabilising effect and an RNA-synthesis stimulating effect on hepatocytes.

Silymarin has free radical capturing powers, silymarin possesses antiperoxidative activity. The pathophysiological process of lipid peroxidation which is responsible for the destruction of cell membranes is interrupted or reduced. Furthermore, in liver cells, which have already sustained damage, silymarin stimulates protein synthesis and normalises phospholipid metabolism.

The enhancement of protein synthesis by silymarin is due to its stimulation of RNA polymerase I, an enzyme which is located in the nucleus. This leads to increased formation of ribosomal RNA and structure and function proteins (enzymes) are therefore synthesised in greater amounts.

Pharmacokinetic properties

The principal constituent of silymarin is silibinin. Clinical investigations show that after its absorption in the digestive tract, it is excreted mainly in the bile (> 80 % of the amount absorbed).

As metabolites, glucoronides and sulphates have been demonstrated in the bile, silibinin is assumed to be reabsorbed after being deconjugated, and then enters into an enterohepatic circulation, as has been shown in experimental animals. Blood levels are low and renal elimination is small. The absorption half-life is 2.2 hours and the elimination half-life 6.3 hours.

When silymarin is given in therapeutic doses (140 mg three times daily), the levels of silibinin found in human bile are the same after repeated doses and after a single dose. The results show that silibinin does not accumulate in the body.

After repeated administration of silymarin in doses of 140 mg three times daily, biliary elimination reaches a steady state at 2 days.

INDICATIONS

Legalon® forte is indicated as an aid in the treatment of alcohol induced liver disease.

Note: **Legalon®** forte is not suitable for treating cases of acute poisoning.

CONTRA-INDICATIONS

Leaglon® forte should not be administered in cases of known hypersensitivity against milk thistle fruits, other composites or any of the excipients.

WARNINGS

The treatment with **Legalon®** forte does not serve as a substitute for the abstention from the cause of liver damage (e.g. alcohol).

If icterus (light to dark yellow tinge of the skin, yellow discoloration of the white of the eye) occurs, the doctor is to be consulted.

There is no data available concerning the use of **Legalon®** forte in children. Therefore, it should not be used in children under the age of 12 years.

INTERACTIONS

No interactions with any other medicinal products or any other form of interaction are known.

PREGNANCY AND LACTATION

Safety and efficacy have not been established during pregnancy and lactation. There are no adequate data from the use of **Legalon®** forte in pregnant or lactating women. Therefore, in these circumstances **Legalon®** forte should not be administered.

DOSAGE AND DIRECTIONS FOR USE

1 capsule three times daily, corresponding to 420 mg (324,6 mg) of silymarin daily.

The capsules are to be swallowed whole and unchewed with an appropriate amount of liquid.

The doctor will decide on the duration of the treatment.

Paediatric patients

Legalon® forte is not recommended for use in children under the age of 12 years, due to insufficient data on safety and efficacy.

SIDE EFFECTS AND SPECIAL PRECAUTIONS

Side effects

Legalon® forte can have side effects.

Very common (≥ 1/10); common (≥ 1/100, < 1/10); uncommon (≥ 1/1 000, < 1/100); rare (≥ 1/10 000, < 1/1000); very rare (≤ 1/10 000), including isolated reports, not known (cannot be estimated from available data).

SYSTEM ORGAN CLASS (MedDRA)	FREQUENCY	ADVERSE EVENT
Immune system disorders	Very Rare	Dyspnoea, hypersensitivity reactions
Gastrointestinal disorders	Rare	Mild laxative effect
Skin and subcutaneous tissue disorders	Very Rare	Rash

Effects on the ability to drive and use machinery

Not known.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

Signs or symptoms of overdosage have not hitherto been observed. The undesirable effects described above can be amplified.

If necessary, symptomatic measures are recommended. In the even of any adverse reaction occurring, consult a doctor or the nearest hospital.

IDENTIFICATION

Brown hard gelatine capsules containing yellow powder.

PRESENTATION

Available in blister strips of 10 packed in collapsible cartons of 30, 60 or 100 capsules.

STORAGE INSTRUCTIONS

Store in tightly sealed containers protected from moisture at room temperature (below 25 ºC).

KEEP OUT OF REACH OF CHILDREN

REFERENCE NUMBER

45/7.4/1132

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138 **DATE OF PUBLICATION OF THE PACKAGE INSERT**

139 02 October 2014