SCHEDULING STATUS S0

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.

Sugar free

List of excipients

Polysorbate 80, povidone, mannitol, sodium starch glycolate, magnesium stearate, iron oxide red E172, iron oxide black 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.

CONTRAINDICATIONS

LEGALON® 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.

For evaluation of undesirable effects, the following terms of frequency are used:
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	FREQUENCY	ADVERSE EVENT
Immune system disorders	Very Rare	Dyspnoea, hypersensitivity reactions
Gastrointestinal disorders	Rare	Mild laxative effect
Skin and subcutaneous tissue disorder	Very Rare	Rash

Effects on the ability to drive and use machinery:
None 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 event 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 at or below 25 °C.
Store in the original container, protected from moisture.
KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER

45/7.4/1132

NAME AND BUSINESS ADDRESS OF THE HOLDER OF CERTIFICATE OF REGISTRATION

Xixia Pharmaceuticals (Pty) Ltd.
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DATE OF PUBLICATION OF THE PACKAGE INSERT

02 October 2014

Mylan

www.mylansa.co.za

SKEDULERINGSTATUS S0

EIENDOMSNAAM EN DOSEERVORM

LEGALON® FORTE kapsules

SAMESTELLING

Elke kapsule bevat: 173,0 mg – 186,7 mg gedroogde ekstrak van melkdisselvrugte wat ooreenstem met 140 mg siliemarien, bereken as siliebinien.
Suikervry

Lys van mengmiddels
Polisorbaat 80, povidoon, mannitol, natriumstyselglikolaat, magnesiumstearaat, ysteroksied rooi E172, ysteroksied swart E172, titaandioksied E171, gelatien, natriumlaurielsulfaat.

FARMAKOLOGIESE KLASSIFIKASIE

A 7.4 Lipotropiese middels

FARMAKOLOGIESE WERKING

Farmakodinamiese eienskappe

Siliemarien het 'n membraan-stabiliserende effek en 'n DNS-sintese stimulerende effek op hepatosiete.

Siliemarien besit vrye-radikaal-opvangkragte, siliemarien besit anti-peroksidatiewe aktiwiteit. Die patofisiologiese proses van lipiedperoksidasie wat verantwoordelik is vir die vernietiging van selmembrane word onderbreek of verminder. Daarbenewens, stimuleer siliemarien proteïensintese en normaliseer dit fosfolipiedmetabolisme in lewerselle wat alreeds beskadig is.

Die versterking van proteïensintese deur siliemarien is as gevolg van sy stimulasie van DNS-polimerase-I, 'n ensiem wat in die nukleus geleë is. Dit lei tot verhoogde vorming van ribosomale DNS en struktuur en funksie-proteïene (ensieme) word dus in groter hoeveelhede gesintetiseer.

Farmakokinetiese eienskappe
Die hoofbestanddeel van siliemarien is siliebinien. Kliniese ondersoeke het aangedui dat dit na absorpsie uit die spysverteringskanaal, hoofsaaklik in gal uitgeskei word (> 80 % van die hoeveelheid wat geabsorbeer word).

Omdat metaboliete, glukuroniede en sulfate in die gal gedemonstreer is, word dit aangeneem dat siliebinien herabsorbeer word nadat dit gedekonjugeer word, en dan 'n enteropatiese sirkulasie binnegaan, soos gedemonstreer kon word in eksperimentele diere. Bloedvlakke is laag en renale eliminasie is min. Die absorpsie halfleeftyd is 2,2 uur en die eliminasie halfleeftyd is 6,3 uur.

Wanneer siliemarien in terapeutiese dosisse gegee word (140 mg drie keer per dag), is die vlakke siliebinien wat in menslike gal opgespoor word, dieselfde na herhaalde dosisse en na 'n enkeldosis. Die resultate dui aan dat siliebinien nie in die liggaam akkumuleer nie.

Na herhaalde toediening van siliemarien in dosisse van 140 mg drie keer per dag, bereik bilière eliminasie die ewewigstoestand na 2 dae.

INDIKASIES

LEGALON® FORTE word aangedui as 'n hulpmiddel in die behandeling van alkohol-geïnduseerde lewersiekte.

Let Wel: **LEGALON® FORTE** is nie vir die behandeling van gevalle van akute vergiftiging, geskik nie.

KONTRA-INDIKASIES

LEGALON® FORTE behoort nie toegedien te word nie in gevalle van bekende hipersensitiwiteit teen melkdisselvrugte, ander samestellings of enige van die mengmiddels.

WAARSKUWINGS

Behandeling met **LEGALON® FORTE** behoort nie te dien nie as 'n vervanging vir geheelonthouding van die oorsaak van lewerskade (bv. alkohol).

Indien ikterus (ligte tot donker kleur van die vel, geel verkleuring van die wit gedeelte van die oog) voorkom, moet die dokter geraadpleeg word.

Daar is geen data oor die gebruik van **LEGALON® FORTE** by kinders beskikbaar nie. Dit behoort dus nie by kinders onder die ouderdom van 12 jaar gebruik te word nie.

INTERAKSIES

Geen interaksies met ander medisinale produkte of enige ander vorm van interaksie is bekend nie.

SWANGERSKAP EN LAKTASIE

Veiligheid en doeltreffendheid tydens swangerskap en laktasie is nie vasgestel nie. Geen toereikende data oor die gebruik van **LEGALON® FORTE** in swanger of lakterende vrouens is beskikbaar nie. Onder hierdie omstandighede behoort **LEGALON® FORTE** dus nie toegedien te word nie.

DOSIS EN GEBRUIKSAANWYSINGS

1 kapsule drie keer daagliks wat ooreenstem met 420 mg (324,6 mg) siliemarien daagliks.

Die kapsules moet heel en nie gekou ingesluk word met 'n geskikte hoeveelheid vloeistof. Die geneesheer sal besluit op die duur van die behandeling.

Pediatriese pasiënte
LEGALON® FORTE word nie vir gebruik by kinders jonger as 12 jaar aanbeveel nie, weens onvoldoende data oor veiligheid en doeltreffendheid.

NEWE-EFFEKTE EN SPESIALE VOORSORGMAATREËLS

Newe-effekte
LEGALON® FORTE kan newe-effekte veroorsaak.

Vir evaluering van ongewenste effekte word die volgende terme van frekwensie gebruik.
Baie algemeen (≥ 1/10); algemeen (≥ 1/100, < 1/10); ongewoon (≥ 1/1 000, < 1/100); seldsaam (≥ 1/10 000, < 1/1 000); baie seldsaam (≤ 1/10 000), insluitend geïsoleerde berigte, nie bekend nie (kan nie van beskikbare data beraam word nie).

SISTEEM – ORGAANKLAS	FREKWENSIE	NADELIGE INSIDENT
Immuunsisteem-versteurings	Baie Seldsaam	Dispnee, hipersensitiwiteits-reaksies
Gastroïntestinale versteurings	Seldsaam	Ligte lakserende effek
Vel- en onderhuidse weefsel-versteurings	Baie Seldsaam	Veluitslag

Effekte op die vermoë om te bestuur en masjiene te gebruik:
Geen bekend nie.

BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VAN DIE BEHANDELING DAARVAN

Tekens of simptome van oordosering is tot op datum nog nie waargeneem nie. Die ongewenste effekte wat hierbo beskryf is, mag versterk word.

Indien nodig, word simptomatiese maatreëls aanbeveel. In 'n geval van enige nadelige reaksies wat mag voorkom, moet 'n geneesheer of die naaste hospitaal geraadpleeg word.

IDENTIFIKASIE

Bruin, harde gelatienkapsules wat 'n geel poeier bevat.

AANBIEDING

Beskikbaar in stulpverpakkingstroke van 10 verpak in voubare kartondose van 30, 60 of 100 kapsules.

BEWARINGSINSTRUKSIES

Bêre teen of benede 25 °C.
Bêre in die oorsponklike houer, beskerm teen vog.
HOU BUITE BEREIK VAN KINDERS.

REGISTRASIENOMMER

45/7.4/1132

NAAM EN BESIGHEIDSADRES VAN DIE HOUER VAN DIE REGISTRASIESERTIFIKAAT

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