

# BETULIN HEPATO

(Betulafarm®)

## USER'S

### Scope of application

It is recommended as dietary food supplement — a source of betulin and flavolignans.

### Composition

extract of holy thistle fruits – 160 mg, birch betulin (birch bark extract) – 40 mg.

**Capsule shell composition** – gelatin, titanium dioxide, ferric oxide.

**Directions for use** – for adults: take 1 capsule per day with food during 3-4 weeks. Repeat the course, if necessary. Consult your doctor before use.

### Contraindications

Idiosyncratic reaction to product ingredients, pregnancy, breast-feeding.

**Size:** 200 mg capsules.

**Shelf life:** 2 years from the date of manufacture.

**Storage conditions:** store in dry place; keep out of reach of children; don't store above +25 °C

TS 9197-003-74779358-15



It is not a drug product.  
Certificate of State Registration

RU.77.99.88.003.E.006253.05.15 dd. May 12, 2015  
"Betulin Hepato" should be sold through specialized stores or pharmacy chain shops.

### Manufacturer

Vitamer LTD., Office III, 1 Orlovo-Davydovskiy Lane, Moscow 129110

Production address: 11 Sovkhoznaya Street, Petushki, Vladimir Region

By order of Betulafarm LTD.,  
5 Lev Tolstoy Street, St. Petersburg,

Claims to be sent to the authorized organization below:  
BetulaFarm LTD., 5 Lev Tolstoy Street, St. Petersburg,  
phone: 8 800 100 1738.

## ADDITIONAL INFORMATION

Detailed information — on the company's web-site: [www.betulin.com](http://www.betulin.com)

## INSTRUCTION

Field of application of betulin and holy thistle extract: they are recommended as a dietary food supplement — a source of betulin, betulin bioflavonoids (lupan, lupeol, lupenon, betulin acetate) and silibinin and can be used at hepatitis of all kinds, cirrhosis of hepatic tissues, biliary dyskinesia and gallstone disease, diseases of gall bladder, bowels, at dystrophy and liver fatty infiltration, at hypernutrition and chronic constipations, for lipid exchange correction. Betulin and holy thistle extract will help people with health-detrimental behavior (smoking, alcoholism, drug abuse) and people, who work in ecologically unfavorable conditions. It removes consequences of toxic damages of liver including consequences of the system chemotherapy in oncologic patients. Betulin and holy thistle extract are also favorable at such diseases, as:

- hepatitis;
- hepatocirrhosis;
- hepatic fibrosis;
- toxic lesion of liver;
- hyperlipidemia;
- hyperchylomicronemia;
- hyperglycinemia;
- hypercholesterolemia;
- Hanot's cirrhosis;
- secondary biliary cirrhosis;
- metabolic imbalance of lipoproteins;
- mental disorders;
- liver impairment.

**Betulin** (lup-20(29)-ene-3 $\beta$ , 28-diol) is widespread, natural compound from the triterpenes group produced from upper birch bark.

**Betulin** is white color powder, odorless, with weak astringent taste. It is oxygen- and sunlight-resistant, non-toxic. Water-insoluble. It is very soluble in organic solvents. High melting temperature of betulin (240-260 °C), stable chemical formula and inert properties of the molecule provide extended storage period without changing properties.

### HEPATOPROTECTIVE ACTION OF BETULIN

Studies of hepatoprotective action of betulin during development of acute hepatitis caused by paracetamol, carbon tetrachloride or ethanol demonstrated its high efficiency in blocking destruction processes of liver cell membranes, suppression of activity of enzyme systems and tissue respiration, reduction of peroxidation of lipids of cellular membranes. Betulin increased synthetic processes in liver cells and restored the biligenic function. Betulin blocked the influence of carbon tetrachloride, which causes necrosis of hepatic cells, inflammatory edema and cellular infiltration.

Betulin impeded the development of necrosis of hepatic cells, hepatic steatosis and accumulation of alcoholic hyaline under the influence of ethyl spirit, i.e. prevented the cirrhosis development. At chronic hepatitis, betulin reduced the

elevated levels of AST, ALT and LDH effectively. It has been established that betulin is able to protect cellular membranes against damaging action of xenobiotics. Prophylactic application of betulin (14 days) in a dose of 10 mg per kilogram of weight prevents the destruction of hepatocytes, inflammatory infiltration, colliquative necrosis, improves the liver biligenic function (the bilification intensity was restored on the 4<sup>th</sup> day after intoxication), protects liver zones with localization of cytochrome P-450. At that, the activity of ALT decreased for 82 %, alkaline phosphatase — for 69 %, content of triglycerides in blood — for 62 %, decrease of triglycerides in liver tissue — for 55 %. Betulin stabilizes membranes of mitochondrions (cell energy depot), preventing their damage as a result of oxidation processes, starts the natural apoptosis process not allowing the mitochondrial DNA escaping from the damaged cell and in so doing to initiate the autoimmune process (inflammation).

Hence, betulin counterbalances intracellular homeostasis at the expense of stabilizing of plasma membrane and membranes of intracellular organoids, as well as activating the main detoxicating enzyme — cytochrome P-450. The ability of betulin in conditions of hypoxia — a state accompanying the toxic liver damage — to increase the level of cytochrome P-450 in it and relative activity of monooxygenases indicates about this. Betulin as a natural hepatoprotector is effective at acute and chronic liver damages of any etiology including complicated by cholestasis.

Betulin demonstrated the efficiency at viral diseases of liver (hepatitis A, B and C) as well, during chemotherapy and radiation therapy of oncologic patients, at alcohol-induced liver injuries (as a prophylactic drug), at injuries, burns, surgical operations, particularly with general anesthesia. Application of betulin in the complex therapy of hepatitis and hepatocirrhosis results in the acceleration of clinical recovery and renewal of physical working capacity. The absence of toxicity and side effects even at the prolonged application of betulin and heavy damage of liver parenchyma is an important factor of application of betulin.

#### PHARMACOKINETICS

The kinetics of betulin secretion in blood at single oral introduction of betulin suspension was studied during experiments (calculated dose is 200 mg/kg). The curve of betulin detectability in blood has the specific “breaking wave” configuration. The average betulin concentration in blood plasma after the first hour was 55 µg/ml. At that, the preparation entering into the blood took place with appr. 10 minutes delay. The peak of betulin concentration is achieved by the 2<sup>nd</sup> hour and it is equal to 95 µg/ml. Then from the 2<sup>nd</sup> to the 4<sup>th</sup> hour the betulin content in blood is lowered to 75.6 % and by 16 hours the preparation concentration makes 9 % of the maximum.



#### SAINT-MARY-THISTLE EXTRACT

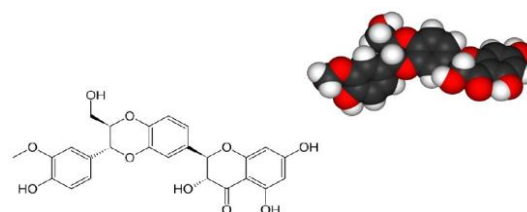
**Hepatotropic action of Saint-Mary-thistle extract:** bioactive compounds in the Saint-Mary-thistle extract interact with free radicals in liver and reduce their toxicity. While interrupting the lipid peroxidation process they prevent further destruction of cellular structures. In damaged hepatocytes they stimulate the synthesis of structural and functional proteins and phospholipids (at the expense

of specific stimulation of RNA polymerase A), stabilize cellular membranes, prevent the loss of cellular components and intracellular enzymes (transaminases), accelerate the liver cell regeneration. They inhibit penetration of some hepatotoxic substances (poisons of death cap mushroom) into cells. They improve general well-being of patients with liver diseases, diminish subjective complaints and normalize lab test values (activity of transaminases, gamma glutamine transferase, alkaline phosphatase, bilirubin level). The prolonged use of holy thistle extract reliably increases the survival fraction of patients with hepatocirrhosis.

#### PHARMACOKINETICS

Absorption is low and slow (half-absorption period is 2.2 h). It is exposed to the enterohepatic cycle and metabolized in liver by conjugation, T=0.5-6 h. Excretion is mainly with bile in the form of glucuronids and sulfates, to a small extent with urine. It does not cumulate. After repeated administrations by 140 mg 3 times per day, stable concentration is achieved. The main acting substance in the holy thistle extract is silibinin.

#### SILIBININ



(2R,3R)-3,5,7-trihydroxy-2-[(2R,3R)-3-(4-hydroxy-3methoxyphenyl)-2-(hydroxymethyl) -2,3-dihydrobenzo[b][1,4]dioxin-6-yl]chroman-4-one

Hepatotropic action of silibinin — phytoenous hepatoprotector extracted from Saint-Mary-thistle fruits. Silibinin accelerates the liver cell regeneration, some toxins destroy lipids of cellular membranes like free radicals. Silibinin is able to oppress an enzyme, which strengthens the peroxidation process and that makes it an ideal protection mean for liver against noci-influence of alcohol, cigarette smoke, medicines and other toxic substances. Silibinin reduces the bilirubin content, reduces compromised liver function, occurring in workers engaged in production of pesticides, stops destroying influence of siliceous dust, which affects respiratory tracts. In addition, silibinin is highly efficient in case of liver damage caused by heavy metals contained in water, air and foodstuffs. Silibinin strengthens the bile outflow and bile flow, improves the skin health at hepatic disorders.

#### PHARMACOKINETICS

Silibinin has low absorption, it is metabolized in liver by conjugation, T=0.5-6 h. Excretion is mainly with bile in the form of glucuronids and sulfates. Enterohepatic circulation takes place. The preparation is not cumulated in the body. After repeated administrations by 140 mg 3 times per day stable elimination level is achieved with bile.

### INDICATIONS AND USAGE

Betulin and holy thistle extract can be prescribed as a powerful prophylactic complex at hepatitis of all kinds, cirrhosis of at hepatitis of all kinds, cirrhosis of hepatic tissues, biliary dyskinesia and gallstone disease, diseases of gall bladder, bowels, at dystrophy and liver fatty infiltration, at hypernutrition and chronic constipations, for lipid exchange correction. The complex of betulin and holy thistle extract will help people with health-detrimental behavior (smoking, alcoholism, drug abuse) and people, who work in ecologically unfavorable conditions. It removes consequences of toxic damages of liver including consequences of the system chemotherapy in oncologic patients.

- hepatitis;
- hepatocirrhosis;
- hepatic fibrosis;
- toxic lesion of liver;
- hyperlipidemia;
- hyperchylomicronemia;
- hyperglycinemia;
- hypercholesterolemia;
- Hanot's cirrhosis;
- secondary biliary cirrhosis;
- metabolic imbalance of lipoproteins;
- mental disorders;
- liver impairment.

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Duly authorized signatory

Natalya Yu. Gashkova