Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Ursofalk 250 mg Hard capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 250mg of ursodeoxycholic acid.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Capsule, hard

Product imported from Spain
White opaque hard gelatin capsules containing a white compressed powder or granules.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For the dissolution of cholesterol gallstones in functioning gallbladders with or without prior extracorporeal shock wave lithotripsy.

Primary biliary cirrhosis (PBC) stages I – III.

4.2 Posology and method of administration

Ursofalk capsules are for oral administration.

The following daily dose is recommended for the various indications:

Primary biliary cirrhosis (PBC) stages I – III:
The daily dose depends on body weight, and ranges from 3 to 7 capsules (14 ± 2 mg ursodeoxycholic acid per kg of body weight).

For the first 3 months of treatment, Ursofalk capsules should be taken divided over the day.
With improvement of the liver values the daily dose may be taken once daily in the evening.

Body weight (kg)	Daily dose (mg/kg BW)	Ursofalk capsules			
		first 3 months			subsequently
		Morning	Midday	Evening	Evening (1 x daily)
47-62	12-16	1	1	1	3
63-78	13-16	1	1	2	4
79-93	13-16	1	2	2	5
94-109	14-16	2	2	2	6
Over 110		2	2	3	7

The capsules should be swallowed whole with some liquid. Care should be taken to ensure that they are taken regularly.

The use of Ursofalk capsules in primary biliary cirrhosis may be continued indefinitely.

In patients with primary biliary cirrhosis, in rare cases the clinical symptoms may worsen at the beginning of treatment, e.g. the itching may increase. Should this occur, therapy should be continued with 1 capsule daily, and the therapy gradually increased (increase of the daily dose weekly by 1 capsule) until the dose indicated in the respective dosage regimen is reached again.

Dissolution of Gallstones:

Adults: The usual dose is 10 – 12mg/kg/day to be taken in the evening, i.e. 750mg, daily in the evening.

All indications

Children: Not recommended.

4.3 Contraindications

Ursofalk should not be used in patients with:

- Acute inflammation of the gall bladder or biliary tract
- occlusion of the biliary tract (occlusion of the common bile duct or a cystic duct)
- frequent episodes of biliary colic
- radio-opaque calcified gallstones
- impaired contractility of the gall bladder
- hypersensitivity to bile acids or any excipient of the formulation

4.4 Special warnings and precautions for use

Ursofalk capsules should be taken under medical supervision.

During the first 3 months of treatment, liver function parameters AST (SGOT), ALT (SGPT) and γ - GT should be monitored by the physician every 4 weeks, thereafter every 3 months.
Apart from allowing for identification of responders and non-responders in patients being treated for primary biliary cirrhosis, this monitoring would also enable early detection of potential hepatic deterioration, particularly in patients with advanced stage primary biliary cirrhosis.

When used for dissolution of cholesterol gallstones:
In order to assess therapeutic progress and for timely detection of any calcification of the gallstones, depending on stone size, the gall bladder should be visualised (oral cholecystography) with overview and occlusion views in standing and supine positions (ultrasound control) 6-10 months after the beginning of treatment.

If the gall bladder cannot be visualised on X-ray images, or in cases of calcified gallstones, impaired contractility of the gall bladder or frequent episodes of biliary colic, Ursofalk® capsules should not be used.

When used for treatment of advanced stage of primary biliary cirrhosis:
In very rare cases decompensation of hepatic cirrhosis has been observed, which partially regressed after the treatment was discontinued.

If diarrhoea occurs, the dose must be reduced and in cases of persistent diarrhoea, the therapy should be discontinued.

4.5 Interaction with other medicinal products and other forms of interaction

Ursofalk capsules should not be administered concomitantly with colestyramine, colestipol or antacids containing aluminium hydroxide and/or smectite (aluminium oxide), because these preparations bind ursodeoxycholic acid in the intestine and thereby inhibit its absorption and efficacy.

Should the use of a preparation containing one of these substances be necessary, it must be taken at least 2 hours before or after Ursofalk capsules.

Ursofalk capsules can increase the absorption of ciclosporin from the intestine. In patients receiving ciclosporin treatment, blood concentrations of this substance should therefore be checked by the physician and the ciclosporin dose adjusted if necessary.

In isolated cases Ursofalk capsules can reduce the absorption of ciprofloxacin.

Ursodeoxycholic acid has been shown to reduce the plasma peak concentrations (C_{max}) and the area under the curve (AUC) of the calcium antagonist nitrendipine.

An interaction with a reduction of the therapeutic effect of dapsone was also reported.

These observations together with in vitro findings could indicate a potential for ursodeoxycholic acid to induce cytochrome P450 3A enzymes. Controlled clinical trials have shown, however, that ursodeoxcholic acid does not have a relevant induction effect on cytochrome P450 3A enzymes.
Oestrogenic hormones and blood cholesterol lowering agents such as clofibrate may increase biliary lithiasis, which is a counter –effect to ursodeoxycholic acid used for dissolution of gallstones.

4.6 Fertility, pregnancy and lactation

There are no adequate data on the use of ursodeoxycholic acid, particularly in the first trimester of pregnancy. Animal studies have provided evidence of a teratogenic effect during the early phase of gestation (see section 5.3, Toxicity to reproduction). Ursofalk capsules must not be used during pregnancy unless clearly necessary. Women of childbearing potential should be treated only if they use reliable contraception: non-hormonal or low-oestrogen oral contraceptive measures are recommended. However, in patients taking Ursofalk for dissolution of gallstones, effective non-hormonal contraception should be used, since hormonal oral contraceptives may increase biliary lithiasis.

The possibility of a pregnancy must be excluded before beginning treatment.

It is not known whether ursodeoxycholic acid passes into breast milk. Therefore, Ursofalk capsules should not be taken during lactation. If treatment with Ursofalk is necessary, the infant should be weaned.

4.7 Effects on ability to drive and use machines

No effects on ability to drive and use machines have been observed.

4.8 Undesirable effects

The evaluation of undesirable effects is based on the following frequency data:
Very common (≥ 1/10)
Common (≥ 1/100 to < 1/10)
Uncommon (≥ 1/1,000 to < 1/100)
Rare (≥1/10,000 to < 1/1,000)
Very rare / Not known (< 1/10,000 /cannot be estimated from available data)

Gastrointestinal disorders:
In clinical trials, reports of pasty stools or diarrhoea during ursodeoxycholic acid therapy were common.
Very rarely, severe right upper abdominal pain has occurred during the treatment of primary biliary cirrhosis.

Hepatobiliary disorders:
During treatment with ursodeoxycholic acid, calcification of gallstones can occur in very rare cases.
During therapy of the advanced stages of primary biliary cirrhosis, in very rare cases decompensation of hepatic cirrhosis has been observed, which partially regressed after the treatment was discontinued.

Skin and subcutaneous disorders:
Very rarely, urticaria can occur.

4.9 Overdose

Diarrhoea may occur in cases of overdose. In general, other symptoms of overdose are unlikely because the absorption of ursodeoxycholic acid decreases with increasing dose and therefore more is excreted with the faeces. No specific counter-measures are necessary and the consequences of diarrhoea should be treated symptomatically with restoration of fluid and electrolyte balance.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Ursodeoxycholic acid is a bile acid. It affects concentration of cholesterol in bile. Furthermore, ursodeoxycholic acid can prevent cholestasis and cellular lesions induced by biliary obstruction or bile acid administration. In addition, ursodeoxycholic acid has a direct protective action on liver cell membranes by blocking bile acid receptors or by the incorporation of ursodeoxycholic acid into the liver cell membrane.

5.2 Pharmacokinetic properties

Following oral administration, ursodeoxycholic acid is absorbed, conjugated in the liver and excreted in bile. It is converted by bacteria to lithocholic acid and it undergoes enterohepatic recycling.

5.3 Preclinical safety data

No further relevant information other than that, which is included in other sections of the Summary of Product Characteristics.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maize starch
Magnesium stearate
Colloidal silica

Capsule shell
Titanium dioxide (e171)
Gelatin
Sodium lauryl sulfate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

The shelf life expiry date for this product shall be the date shown on each blister and outer package of the product on the market in the country of origin.

6.4 Special precautions for storage

Do not store above 25ºC.
Keep the capsules in the original package in order to protect from light and moisture.

6.5 Nature and contents of container

PVC/Aluminium blister packs packed in cardboard cartons to contain 100 capsules (10 strips each containing 10 capsules).

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

Not applicable.

7 PARALLEL PRODUCT AUTHORISATION HOLDER

LTT Pharma Limited
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8 PARALLEL PRODUCT AUTHORISATION NUMBER

PPA 1562/31/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 14th January 2011

10 DATE OF REVISION OF THE TEXT

November 2012