1.3 PRODUCT INFORMATION

1.3.1 Summary of product characteristics (SmPC)

Provided in the following pages.

SUMMARY OF PRODUCT CHARACTERISTICS

(PRODUCT DATA SHEET)

1. Name of the Medicinal Product:

1.1 Product Name: URSOLIV 250

1.2 Strength: Please see the product composition

1.3 Pharmaceutical Dosage Form:

2. Quality and Quantitative Composition: Hard capsule

2.1 Qualitative Declaration

2.2 Quantitative Declaration

Composition	Quantity per capsule (mg)
Active Substance	
Ursodeoxycholic acid	250.00
Excipients	
Corn Strarch	86.60
Starch 1500	18.00
Aerosil 200	1.80
Magnesium Stearate Pharma grad	3.60
Purified water*	q.s
Gelatin capsule size 0	98.00

3. Pharmaceutical Form: White to off-white powder filled in size “0” oblong opaque white color hard gelatin shell capsule.

4. Clinical Particulars:

4.1 Therapeutic indications:

- Dissolution of gallstones in patients with radiolucent, noncalcified, gallbladder stones less than 20 mm diameter in whom elective cholecystectomy would be undertaken except for the presence of increasedsurgical risk due to systemic disease, advanced age, idiosyncratic reaction to general anesthesia, or forpatients who refuse surgery.
- Prevention of gallstone formation in obese patients experiencing rapid weight loss.
- Compensated primary biliary cirrhosis

- Chronic cholestatic syndrome various liver lesions.

4.2 Posology and method of administration:

Gallstones Dissolution :

The recommended oral dose for treatment of gallstone disease is 8-10 mg/kg/day given in 2 or 3 divided doses with meals.

Duration of therapy 6-12 months. After complete dissolution, it is recommended that Ursoliv be continued for at least 3 months to promote dissolution of particles that are too small to image.

Gallstone Prevention :

To prevent gallstone formation in obese patient experiencing rapid weight loss the recommended dose is 800 mg twice a day with meals.

Cholestatic liver diseases :

The recommended oral dose for treatment of cholestatic liver diseases is 13-15 mg/kg/day given in 2 divided doses with meals.

Primary biliary cirrhosis :

The daily dose of 10-15 mg/kg/day in divided dose.

Body weight	Daily dose	Morning	Afternoon	Evening
Up to 60 kg	2 caps	1	-	1
60-80 kg	3 caps	1	1	1
80-100 kg	4 caps	1	1	2

4.3 Contraindications:

Ursoliv must not be used in the presence of :

- Allergy to bile acids
- Patients with gallstone complications such as biliary-gastrointestinal fistula, biliary obstruction, cholangitis, cholecystitis, pancreatitis or frequent biliary colic.

Ursoliv is ineffective for the dissolution of calcified and pigment gallstones and is of no value in patients without a patent and functioning gallbladder.

4.4 Special warning and precautions for use:

Use in pediatrics :

Safety and efficacy have not been established.

Liver tests :

Patients given ursodeoxycholic acid should have SGPT (ALT), SGOT(AST), GGT, ALP and bilirubin measured at the initiation of therapy and thereafter as indicated by the particular clinical circumstances. Monitoring of serum values is recommended upon initiation of treatment, every 1 to 3 months for the first 3 months of treatment (depending on the indication for use), and then every 6 months during treatment; ursodeoxycholic acid must be discontinued if increased values persist.

4.5 Pregnancy & Lactation: Should not be used during pregnancy and lactation without medical advice.

4.5 Side effects: May cause allergy, cholecystitis, leucopenia, peptic ulcer and urinary tract infection.

4.6 Drug Interactions:

Should not be taken at the same time as antacids containing aluminium, cholestyramine, colestipol, antihyperlipidemics, especially clofibrate, estrogens, neomycin, oral contraceptives or progestins as these preparations bind ursodeoxycholic acid in the intestine, thus impairing absorption and efficacy.

4.7 Overdose & Treatment:

No cases of ursodeoxycholic acid overdose have been reported.

The most likely manifestation of severe overdose with ursodeoxycholic acid would probably be diarrhea, which should be treated symptomatically.

5. Pharmacological Properties:

5.1 Pharmacodynamics Properties:

The mechanism of ursodeoxycholic acid is anticholelithic action is not completely understood, it is known that when administered orally ursodeoxycholic acid is concentrated in bile and decreases biliary cholesterol saturation by inhibiting its intestinal absorption. The reduced cholesterol saturation permits the gradual solubilization of cholesterol from gallstones, resulting in their eventual dissolution.

Ursodeoxycholic acid increases bile flow. In chronic cholestatic liver disease, ursodeoxycholic acid appears to reduce the detergent properties of the bile salts, thus reducing their cytotoxicity. Also, ursodeoxycholic acid may protect liver cells from the damaging activity of toxic bile acids (e.g., lithocholate, deoxycholate, an chenodeoxycholate), which increase in concentration in patients with chronic liver disease.

5.2 Pharmacokinetic Properties:

Ursodeoxycholic acid is absorbed from the small bowel (about 90% of dose). Ursodeoxycholic acid is extensively bound to plasma proteins. Hepatic (first-pass hepatic clearance). Exogenous ursodeoxycholic acid is metabolized in the liver to its taurine and glycine conjugates. The resulting conjugates are secreted into bile. Time to peak concentration is 1 to 3 hour.

The half life of administered ursodeoxycholic acid is 3.5-5.8 days. The excretion of ursodeoxycholic acid is primarily fecal; very small amounts are excreted into urine. Small amount of unabsorbed ursodeoxycholic acid passes into the colon where it undergoes bacterial degradation (7-dehydroxylation); resulting lithocholic acid is partly absorbed from the colon but is sulfated in the liver and rapidly eliminated in the feces as the sulfolithocholyl glycine or sulfolithocholyl taurine conjugate.

5.3 Preclinical Safety Data: Not applicable

6. Pharmaceutical Particulars:

6.1 List of excipients:

Corn Strarch	86.60	mg
Starch 1500	18.00	mg
Aerosil 200	1.80	mg
Magnesium Stearate Pharma grad	3.60	mg
Purified water*	q.s.	
Gelatin capsule size 0	98.00	mg

6.2 Shelf life: 3 years from manufacturing date.

6.3 Special precautions for storage: Store below 25 °C in a dry place, away from direct sunlight. Do not refrigerate.

6.4 Nature and contents of container:

Aluminium foil : Aluminium foil

Outer carton : Printed cardboard carton

7. Marketing Authorization Holder:

MEGA LIFESCIENCES Public Company Limited

384 Moo4, Patana 3 Road, Bangpoo Industrial Estate, Soi 6

Preaksa, Muang Samutprakarn

Samutprakarn 10280, Thailand

8. Marketing Authorization Numbers:

9. Date of first authorization / renewal of the authorization:

10. Date of revision of the text: