For the Use of Registered Medicinal Practitioners or a Hospital or a Laboratory only

(Ursodeoxycholic Acid Tablets BP**)**

URSOKEM

1. Name of the medicinal product

URSOKEM 75 DT
URSOKEM 150
URSOKEM 300
URSOKEM 600

2. Qualitative and quantitative composition

URSOKEM 75 DT

Each Dispersible Tablet contains,
Ursodeoxycholic Acid BP 75 mg

URSOKEM 150

Each Film-Coated Tablet contains,
Ursodeoxycholic Acid BP 150 mg

URSOKEM 300

Each Film-Coated Tablet contains,
Ursodeoxycholic Acid BP 300 mg

URSOKEM 600

Each Film-Coated Tablet contains,
Ursodeoxycholic Acid BP 600 mg

3. Pharmaceutical form

Dispersible Tablets
Film coated Tablets

4. Clinical particulars

4.1 Therapeutic indications

URSOKEM tablets are indicated in the treatment of primary biliary cirrhosis (PBC) and for the dissolution of small to medium sized radiolucent, cholesterol-rich gall-stones in patients with a functioning gall bladder.

Cholesterol stones coated with calcium or stones composed of bile pigments are not dissolved by ursodeoxycholic acid. URSOKEM has a particular place in the treatment of patients in whom surgery is contraindicated or who are anxious to avoid surgery.

Paediatric population

Hepatobiliar disorder associated with cystic fibrosis in children aged 6 years to less than 18 years.

4.2 Posology and method of administration

URSOKEM tablets are for oral administration.
To be taken with a drink of water.

Primary Biliary Cirrhosis

Adults and Elderly: 10 - 15mg ursodeoxycholic acid (UDCA) per kg per day in two to four divided doses.

Children: Dosage should be related to bodyweight.

Dissolution of gallstones

Adults and Elderly:

The usual dose is 6 - 12mg/kg/day either as a single night time dose or in divided doses. This may be increased to 15mg/kg/day in obese patients, if necessary.
The duration of treatment may be up to two years, depending on the size of the stone(s), and should be continued for three months after the apparent dissolution of the stone(s).
Children: Dosage should be related to bodyweight.
Paediatric population
Children with cystic fibrosis aged 6 year to less than 18 years: 20 mg/kg/day in 2-3 divided doses, with further increase to 30 mg/kg/day if necessary.

4.3 Contraindications

Ursodeoxycholic acid should not be used in patients:
1. with radio-opaque calcified gall-stones,
2. with acute inflammation of the gall bladder or biliary tract.
3. with occlusion of the biliary tract (occlusion of the common bile duct or a cystic duct)
4. with frequent episodes of biliary colic
5. with impaired contractability of the gall bladder
6. with hypersensitivity to bile acids or any excipient of the formulation
7. who are pregnant or breastfeeding, or in women who may become pregnant.
8. with chronic liver disease, peptic ulcers or in those with inflammatory diseases of the small intestine and colon.

Paediatric population
Unsuccessful portoenterostomy or without recovery of good bile flow in children with biliary atresia

4.4 Special warnings and precautions for use

Ursodeoxycholic acid should be taken under medical supervision.
During the first 3 months of treatment, the 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 the 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, ursodeoxycholic acid 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.
Patients with rare hereditary problems of galactose intolerance, the Lapp lactose deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Ursodeoxycholic acid should not be administered concomitantly with charcoal, 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 ursodeoxycholic acid.
Ursodeoxycholic acid 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 ursodeoxycholic acid 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 ursodeoxycholic acid does not have a relevant inductive effect on cytochrome P450 3A enzymes.
Oral contraceptives, 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 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. Ursodeoxycholic acid must not be used during pregnancy.Treatment should be discontinued immediately if pregnancy occurs and medical advice sought.
Women of childbearing potential should be treated only if they are using reliable contraception: non-hormonal or low-oestrogen oral contraceptive measures are recommended. However, in patients taking ursodeoxycholic acid 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, ursodeoxycholic acid should not be taken during lactation. If treatment with ursodeoxycholic acid is necessary, breastfeeding must be discontinued.

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.
Ursodeoxycholic acid may give rise to nausea and vomiting. The frequency of these effects are not known.
Hepatobiliary disorders:
During treatment with ursodeoxycholic acid, calcification of gallstones can occur in very rare cases making them unable to be dissolved by bile acid therapy and resulting in surgery for some patients**.**
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 subcutaneaous disorders:
Very rarely, urticaria can occur.
Ursodeoxycholic acid may give rise to pruritus. The frequency of this effect is not known.

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

When given by mouth, ursodeoxycholic acid reduces the ratio of cholesterol to bile salts plus phospholipids in bile, causing desaturation of cholesterol saturated bile. The exact mechanism of action has not been fully elucidated.
Paediatric population
Cystic fibrosis
From clinical reports long-term experience up to 10 years and more is available with UCDA treatment in paediatric patients suffering from cystic fibrosis associated hepatobiliary disorders (CFAHD). There is evidence that treatment with UCDA can decrease bile duct proliferation, halt progression of histological damage and even reverse hepato-biliary changes if given at early stage of CFAHD. Treatment with UDCA should be started as soon as the diagnosis of CFAHD is made in order to optimize treatment effectiveness.

5.2 Pharmacokinetic properties

Ursodeoxycholic acid is absorbed from the gastro-intestinal tract and undergoes first pass metabolism and enterohepatic recycling. It is partially conjugated in the liver before being excreted into bile and undergoing 7-α-dehydroxylation to lithocholic acid, some of which is excreted directly in the faeces. The rest is absorbed and mainly conjugated and sulphated by the liver before excretion in the faeces.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to those already included in other sections.

6. PHARMACEUTICAL PARTICULARS

6.1 Shelf life

24 months

6.2 Special precautions for storage

Store in a cool, dry place. Protect from light.

6.3 Nature and contents of container

Pack of 10's

7. Marketed By

ALKEM

Alkem Laboratories Ltd.
ALKEM HOUSE,
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Mumbai - 400 013. INDIA.

8. DATE OF REVESION OF TEXT

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