Only for the use of Medical Professionals

Bilicir®

Ursodeoxycholic Acid

Description

Bilicir® is a preparation of Ursodeoxycholic Acid, which is a naturally occurring hydrophilic bile acid, derived from cholesterol, is present as a minor fraction of the total human bile acid pool. **Bilicir®** increases this fraction in a dose related manner, to become the major biliary acid, (replacing/displacing toxic concentrations of endogenous hydrophobic bile acids that tend to accumulate in cholestatic liver disease). In addition to the replacement and displacement of toxic bile acids, other mechanisms of action include cytoprotection of the injured bile duct epithelial cells (cholangiocytes) against toxic effects of bile acids, inhibition of apoptosis of hepatocytes, immunomodulatory effects, and stimulation of bile secretion by hepatocytes and cholangiocytes. **Bilicir®** also reduces the ratio of cholesterol to bile salts plus phospholipids in bile, causing desaturation of cholesterol saturated bile.

Indications

Bilicir® is indicated-

- In the treatment of Primary Biliary Cirrhosis (PBC)
- For the dissolution of small to medium sized radiolucent, cholesterol-rich gallstones in patients with a functioning gall bladder.
- For the prevention of the gallstone formation in obese patients experiencing rapid weight loss.

Dosage and administration

Primary Biliary Cirrhosis (PBC):

The recommended adult dosage for **Bilicir®** in the treatment of PBC is 13 to 15 mg/kg/day administered in two to four divided doses with food.

Dissolution of gallstones:

Adults and Elderly: The usual dose is 6- 12 mg/kg/day either as a single night time dose or in divided doses. This may be increased to 15 mg/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).

Gallstone prevention:

The recommended dosage for gallstone prevention in patients undergoing rapid weight loss is 600 mg per day (300 mg b.i.d.).

Elderly:

There is no evidence to suggest that any alteration in the adult dose is needed but the relevant precautions should be taken into account.

Children with cystic fibrosis (6 years to < 18 years):

20 mg/kg/day in 2-3 divided doses, with further increase to 30 mg/kg/day if necessary.

Use in special populations

Patients with hepatic and renal impairment:

No specific dosage recommendations. However, Ursodeoxycholic Acid therapy has not been associated with liver damage.

Pregnancy & 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 unless clearly necessary. Treatment should be discontinued immediately if pregnancy occurs. 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, breast feeding must be discontinued.

Side effects
The most common side effects are diarrhea, pasty stools and very rare side effects include calcification of the gallstone, urticaria; also reported nausea, vomiting and pruritus.

Contraindications
Ursodeoxycholic Acid is contraindicated in patients with a history of hypersensitivity to it or any of the components of the formulation. It is also contraindicated in patients with radio-opaque calcified gall-stones, acute inflammation of the gall bladder or biliary tract, occlusion of the biliary tract, frequent episodes of biliary colic, impaired contractibility of the gall bladder, chronic liver disease, peptic ulcers or in those with inflammatory diseases of the small intestine and colon.

Precautions
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. If the gall bladder cannot be visualized 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. If diarrhea occurs, the dose must be reduced and in cases of persistent diarrhea, 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.

Drug interactions
Ursodeoxycholic Acid should not be administered concomitantly with charcoal, colestyramine, colestipol or antacids containing aluminium hydroxide and/or smectite (aluminium oxide). Ursodeoxycholic Acid can increase the absorption of ciclosporin from the intestine. 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. Oral contraceptives, estrogenic 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.

Overdose
Diarrhea may occur. 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 diarrhea should be treated symptomatically with restoration of fluid and electrolyte balance. However, ion-exchange resins may be useful to bind bile acids in the intestine. Liver function tests monitoring is recommended.

Pharmaceutical precautions
Store in a cool & dry place. Protect from light. Keep out of the reach of children.

Presentation
Bilicir® 150 Tablet: Each tablet contains Ursodeoxycholic Acid BP 150 mg.
Bilicir® 300 Tablet: Each tablet contains Ursodeoxycholic Acid BP 300 mg.

Package quantities
Bilicir® 150 Tablet: Carton of 50 tablets in blister pack.
Bilicir® 300 Tablet: Carton of 30 tablets in blister pack.

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