UROSODIOL - Actigall® (Ciba)(Rx)

Prescriber Highlights
- Bile acid that may be useful for tx of hepatobiliary disease in dogs/cats. May also be used for cholesterol containing gallstones.
- Contraindicated: rabbits and other hindgut fermenters. Caution: complications associated with gallstones (e.g., biliary obstruction, biliary fistulas, cholecystitis, pancreatitis, cholangitis).
- Adverse effects: appears to be well tolerated in dogs/cats.

Drug Interactions

Chemistry - A naturally occurring bile acid, ursodiol, also known as ursodeoxycholic acid has a molecular weight of 392.6.

Storage/Stability/Compatibility - Unless otherwise specified by the manufacturer, ursodiol capsules should be stored at room temperature (15-30°C) in tight containers.

Pharmacology - After oral administration, ursodiol suppresses hepatic synthesis and secretion of cholesterol. Ursodiol also decreases intestinal absorption of cholesterol. By reducing cholesterol saturation in the bile it is thought that ursodiol allows solubilization of cholesterol-containing gallstones. Ursodiol also increases bile flow and in patients with chronic liver disease it apparently reduces the hepatocyte toxic effects of bile salts by decreasing their detergent action, and may protect hepatic cells from toxic bile acids (e.g., lithocholate, deoxycholate and chenodeoxycholate).

Uses/Indications - In small animals, ursodiol may be useful as adjunctive therapy for the medical management of cholesterol-containing gallstones and/or in patients with chronic liver disease, particularly where cholestasis (bile toxicity) plays an important role.

Ursodiol’s benefit in treating canine or feline hepatobiliary disease is unknown at writing (studies are ongoing), but it may be of help in slowing the progression of inflammatory hepatic disorders, particularly autoimmune hepatitis and acute hepatotoxicity.

Pharmacokinetics - Ursodiol is well absorbed from the small intestine after oral administration. In humans, up to 90% of dose is absorbed. After absorption, it enters the portal circulation. In the liver it is extracted and combined (conjugated) with either taurine or glycine and secreted into the bile. Only very small quantities enter the systemic circulation and very little is detected in the urine. After each entero-hepatic cycle, some quantities of conjugated and free drug undergoes bacterial degradation and eventually most of the drug is eliminated in the feces after being oxidized or reduced to less soluble compounds. Ursodiol detected in the systemic circulation is highly bound to plasma proteins.

Contraindications/Precautions/Reproductive Safety - Ursodiol is contraindicated in rabbits and other hindgut fermenters as it is converted into lithocholic acid (toxic). Patients sensitive to other bile acid products may also be sensitive to ursodiol. The benefits of using ursodiol should be weighed against its risks in patients with complications associated with gallstones (e.g., biliary obstruction, biliary fistulas, cholecystitis, pancreatitis, cholangitis). While ursodiol may be useful in treating patients with chronic liver disease, some patients may experience further impairment of bile acid metabolism.

Ursodiol’s safety during pregnancy has not been unequivocally established, but studies in rats at doses up to 100 times those given therapeutically in humans demonstrated no adversity to fetuses. It is unknown whether the drug enters breast milk, but no problems have thus far been reported and it would unlikely be of concern (due to the very low systemic levels of the drug present).

Adverse Effects/Warnings - While ursodiol use in animals has been limited, it appears to be well tolerated in dogs and cats. Although hepatotoxicity has not been associated with ursodiol therapy, some human patients have an inability to sulfate lithocholic acid (a naturally occurring bile acid and also a metabolite of ursodiol). Lithocholic acid is a known hepatotoxin; veterinary significance is unclear. Diarrhea and other GI effects have rarely been noted in humans taking ursodiol. Ursodiol will not dissolve calcified, radiopaque stones or radiolucent bile pigment stones.

Overdosage/Acute Toxicity - Overdosage of ursodiol would most likely cause diarrhea. Treatment, if required, could include supportive therapy; oral administration of an aluminum-containing antacid (e.g., aluminum hydroxide suspension); gastric emptying (if large overdose) with concurrent administration of activated charcoal or cholestyramine suspension.

Drug Interactions - Aluminum-containing antacids or cholestyramine-resin may bind to ursodiol, thereby reducing its efficacy.
Doses -

Dogs:

For adjunctive treatment of chronic hepatitis:

a) 5 - 15 mg/kg PO divided q12h, with immunosuppressive therapy. (Note: Use of this drug at this dose is preliminary, but promising) (Johnson and Sherding 1994)

b) 10 - 15 mg/kg PO once daily (Leveille-Webster and Center 1995); (Twedt 1999)

c) For use in chronic active hepatitis, fibrosis and cirrhosis. May use as primary or adjunctive therapy. Dose: 11 - 15.4 mg/kg PO either once daily or divided twice daily (Tams 2000)

Cats:

For adjunctive treatment of chronic hepatitis:

a) 10 - 15 mg/kg PO once daily (Leveille-Webster and Center 1995); (Trepanier 1999)

b) For use in chronic active hepatitis, fibrosis and cirrhosis. May use as primary or adjunctive therapy. Dose: 11 - 15.4 mg/kg PO either once daily or divided twice daily. Cats usually get 1/6th of a capsule mixed with a small amount of food. Cats may eat their food if drug sprinkled on top. (Tams 2000)

Monitoring Parameters - 1) Efficacy (ultrasonography for gallstones; improved liver function tests for chronic hepatic disease); 2) Monitoring of SGPT/SGOT (AST/ALT) on a routine basis (in humans these tests are recommended to be performed at the initiation of therapy and at 1 and 3 months after starting therapy; then every 6 months).

Client Information - Because ursodiol dissolves more rapidly in the presence of bile or pancreatic juice, it should be given with food.

Dosage Forms/Preparations/FDA Approval Status/Withholding Times -

Veterinary-Approved Products: None

Human-Approved Products:

Ursodiol Capsules 300 mg; Actigall® (Ciba)(Rx)