Alert	
Indication	Cholestatic liver disease secondary to total parenteral nutrition and other causes. Choledocholithiasis.
Action	Ursodeoxycholic acid is a hydrophilic bile acid which alters bile acid composition, increases bile acid output and bile flow and decreases reuptake of bile products from the gut. May protect liver cells from damaging activity of toxic bile acids in chronic liver disease.
Drug Type	Bile acid
Trade Name	Urso Suspension [Orphan], Ursofalk Suspension [Orphan]
Presentation	50 mg/mL oral suspension 250 mL
Dosage/Interval	10–15 mg/kg/dose every 12 hours.
Route	Oral
Maximum Daily Dose	30 mg/kg
Preparation/Dilution	
Administration	Oral or intragastric tube. Administer undiluted or mixed with a small amount of milk into infant's mouth through a feeding teat or via intragastric tube.
Monitoring	Monitor liver function tests and serum bilirubin. Observe stool colour.
Contraindications	Hypersensitivity to ursodeoxycholic acid. Complete biliary obstruction.
Precautions	
Drug Interactions	Antacids which contain aluminium bind to ursodeoxycholic acid and reduce its absorption.
Adverse Reactions	Ursodeoxycholic acid is well tolerated. Diarrhoea, vomiting
Compatibility	Not applicable
Incompatibility	Not applicable
Stability	Discard 4 months after opening (write date opened on bottle).
Storage	Store below 25°C.
Special Comments	It is important to prevent fat-soluble vitamin deficiency where there is cholestasis. Consider supplementation if required. Also known as UDCA and ursodiol.
Evidence summary	**Neonatal cholestasis** Ursodeoxycholic acid has been used to prevent and/or treat PN-associated cholestasis in high risk neonates. Gokmen et al[2] compared the effectiveness of oral erythromycin versus ursodeoxycholic acid (UDCA) treatment in preventing feeding intolerance and liver function abnormalities in a prospective, double blind, randomised, controlled trial in which three groups of preterm infants (birth weight < 1500 g) were randomised to erythromycin (12.5 mg/kg/per day), UDCA (5 mg/kg every 6 h) or placebo treatment. Full enteral feeding or intestinal failure-associated liver disease were considered as the primary outcome measures. Time to achieve full feeding after beginning the treatment was significantly shorter in the erythromycin group (P = 0.014). γ-glutamyltransferase (GGT) levels in the placebo group were significantly higher than in the intervention groups (P = 0.001). GTT level was slightly lower in UDCA groups than erythromycin. Conclusion: Oral erythromycin was most effective in facilitating enteral feeding and UDCA was most effective in preventing cholestasis in very low birth weight infants. Prophylactic usage of UDCA could be considered in infants with prolonged parenteral nutrition. Arsanoglu et al[3] conducted a prospective, double-blind, placebo-controlled trial to study the efficacy and safety of ursodeoxycholic acid (UDCA) in preterm infants, in terms of its potential impact on fat absorption, advancement of enteral feeding, development of cholestasis, growth, nutritional status and metabolic status. Although fecal fat excretion slightly decreased and achievement of full enteral feeding was earlier in the UDCA group, these differences were not significant. Interestingly, whereas serum γ-glutamyltransferase activity increased during the parenteral nutrition period in the placebo group, there was a constant and significant decrease in

	the UDCA group. This observation warrants further investigation to determine the utility of prophylactic UDCA in preventing cholestasis in infants with prolonged parenteral nutrition. Chen et al[4] conducted a retrospective study on the effect of ursodeoxycholic acid (UDCA) in VLBW infants with PNAC. Patients were classified as treatment group (receiving UDCA within 14 days of onset of cholestasis) or control group (no medical treatment). A total of 30 patients were recruited, including 12 in the treatment group and 18 in the control group. There was a trend in the control group to later onset of cholestasis. The patients who received UDCA therapy with doses of 10 to 30 mg/kg/day had a shorter duration of cholestasis than the control group (62.8 vs 92.4 days, P = 0.006). Furthermore, the peak serum concentrations of direct bilirubin were significantly lower in the treatment group. **Cystic fibrosis related liver disease** While a recent Cochrane review by Cheng et al[5] found inconclusive evidence for the effectiveness of ursodeoxycholic acid, a number of short-term controlled and uncontrolled trials support the beneficial effects of UDCA on liver biochemistry in CF. **Choledocholithiasis (common bile duct stones) in infancy[6]** Symptomatic choledocholithiasis in infancy is not common. Nordin et al reported 3 patients, in whom a combination of ursodeoxycholic acid and antibiotics was used as a treatment paradigm, potentially negating more invasive treatment. All 3 patients had ultrasonography proven choledocholithiasis with concomitant obstructive liver function test. All 3 patients responded with a return to normal-coloured stools within 48 h of combination treatment. Repeat ultrasonography done within 11 days after the first study confirmed complete resolution of choledocholithiasis for all three patients.
References	1. Product Information: Ursofalk Suspension. MIMSOnline. Accessed 18/08/2015. 2. Gokmen T, Oguz SS, Bozdag S, Erdeve O, Uras N, Dilmen U. A controlled trial of erythromycin and UDCA in premature infants during parenteral nutrition in minimizing feeding intolerance and liver function abnormalities. J Perinatol 2012;32(2):123-8. 3. Arslanoglu S, Moro GE, Tauschel HD, Boehm G. Ursodeoxycholic acid treatment in preterm infants: a pilot study for the prevention of cholestasis associated with total parenteral nutrition. J Pediatr Gastroenterol Nutr 2008;46(2):228-31. 4. Chen CY, Tsao PN, Chen HL, Chou HC, Hsieh WS, Chang MH. Ursodeoxycholic acid (UDCA) therapy in very-low-birth-weight infants with parenteral nutrition-associated cholestasis. J Pediatr 2004;145(3):317-21. 5. Cheng K, Ashby D, Smyth RL. Ursodeoxycholic acid for cystic fibrosis-related liver disease. Cochrane Database Syst Rev 2014;12CD000222. 6. Nordin N, Alex G, Clarnette T, Stephens N, Oliver M. Common bile duct stones in infancy: a medical approach. J Paediatr Child Health 2012;48(8):705-9.

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