

The application to the skin of liniments containing turpentine oil may cause irritation and absorption of large amounts may cause some of the effects listed above. Hypersensitivity reactions and local irritation have been reported.

Uses and Administration

Turpentine oil is widely used as a solvent. It is applied topically as a rubefacient. It is an ingredient of many preparations used in respiratory-tract disorders, but is now judged to be neither safe nor effective.

Preparations

BP 2008: White Liniment.

Proprietary Preparations (details are given in Part 3)

Fr.: Ozothine; **Ger.:** Caprisana†; **Port.:** Vicks Vaporub.

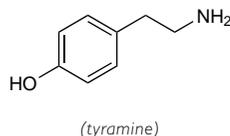
Multi-ingredient: **Arg.:** Atomo Desinflamante C; Bronco Etersan; Fluido; Notoxin; Otolcalmia; Rati Sali Crema; **Austral.:** Goanna Heat Cream; Goanna Salve; Vicks Vaporub; **Austria:** Acimont; Baby Luof; Bronchostop; Carl Baders Divinal; Emser Nasensalbe; Ilon Abszess; Kinder Luof; Leukona-Rheuma-Bad; Luof Balsam; Pe-Ce; Piniment; Rubriment; Salhumin; Scottopect; Trauma-Salbe wärmend; Tussamag; Vulpuran; Wick Vaporub; **Belg.:** Aigis-Spray; Reflexspray; Vicks Vaporub; **Braz.:** A. Curitybina; Aliviol; Analgen†; Angino-Rub; Benegal; Frixopel; Gelflex; Gelofoir; Gelofo; Gelonevral†; Massageol; Mentalof†; Mialgex†; Nevrol; Oleo Elettrico†; Salimetin†; Trauma; Traumagel; Vick Vaporub; **Canad.:** Cal Mo Dol; Cerumol; **Chile:** Balsmac; Leon†; Calorub Nueva Formula; Hansaplast Descongestionante; Mentobalsam; **Cz.:** Ilon Abszess; Viprosal B†; **Fin.:** Vicks Vaporub; **Fr.:** Dinacode†; Lumbalgine; Ozothine; Ozothine a la Diprophylline; Vicks Vaporub; **Ger.:** Em-eukal†; Emser Nasensalbe N†; Erkaltungsbalsam-ratiopharm E Salbe†; Hevertopect; Hevertopect N†; Ilon Abszess; Leukona-Rheuma-Bad N†; Leukona-Rheumasalbe†; Ozothin†; tactu-mobil; Tetesept Baderkonzentrat; Erkaltungs-Bad N†; Trauma-Salbe Rodler 302 N†; Wick Vaporub; **Gr.:** Deep Heat; Farage†-Forte; **India:** Clearwax Flexi-muv; Waxolive; **Indon.:** Opino; Sloan's Liniment; **Israe.:** Deep Heat Rub; Ment-O-Cap; **Ital.:** Capsolin; Vicks Vaporub; **Malaysia:** Thermanol; **Neth.:** Luof Verkoudheidsbalsem; Luof Verkoudheidsbalsem (voor babies); Luof Verkoudheidsbalsem (voor Kinderen); Vicks Vaporub; **NZ:** Vicks Vaporub; **Pol.:** Analgol; Analgol; Capsigel N; Deep Heat†; Derhotil†; Dip Hot; Herbolon; Inhalol; Neo-Capsiderm; Pulmonil†; Reumatik; Rub-Arom; Wick Vaporub; **Port.:** Balsamo Analgesico Basi; Balsamo Analgesico Labesaf†; Calicida Indiano; Freima†; Lauromentol†; **Rus.:** Capsicam (Капсикам); Carmolis Fluid (Кармолис Жидкость)†; Doktor Momm (Доктор Мом); Olimetin (Олиметин)†; Suprima-Plus (Суприма-Плюс); Viprosal B (Випросал В); **S.Afr.:** Balsem Sulphuris; Deep Heat Rub; Haarlemensis; Puma Balm; Respsiniflers; Sloan's Liniment Rub; Vicks Vaporub; Woodwards Inhalant; **Spain:** Dologex†; Embrocacion Gras; Linimento Klar†; Masagit; Oterocerm; Reflex; Termosan; **Swed.:** Vicks Vaporub†; **Switz.:** Aiginex†; Baume du Chale†; Carmol; Cerumenol; Eucapinol; Frixo-Dragon Vert†; Knobel Huile N; Makaphyt Baume†; Massorax†; Pinimenthol†; PO-HO bleu; Pommade au Baume; Vicks Vaporub N; **Thai.:** Stopain; Tiffyrub†; **Turk.:** Algo-Wax; Bugumentol; Buguseptil; Capsalgine; Gelocaps; Kataljin; Vicks Vaporub; **UK:** Deep Heat Rub; Dragon Balm; Eillmans; Goddards Embrocation; Gonne Balm; Modern Herbals Muscular Pain; Nasciodine; Nine Rubbing Oils; Vicks Vaporub; Waxwanet; **USA:** Vicks Vaporub; **Venez.:** Friction Aromatica.

Tyramine Hydrochloride ⊗

Tiramina, hidroclocloro de; *p*-Tyramine Hydrochloride; Tyrosamine Hydrochloride. 4-Hydroxyphenethylamine hydrochloride; 4-(2-Aminoethyl)phenol hydrochloride.

$C_8H_{11}NO \cdot HCl = 173.6$.

CAS — 51-67-2 (tyramine); 60-19-5 (tyramine hydrochloride).



Profile

Tyramine hydrochloride is a sympathomimetic with indirect effects on adrenergic receptors. It has been given orally or by injection in the tyramine pressor test for the investigation of monoamine oxidase inhibitory activity or amine uptake blocking activity. It has also been used in studies of physiological and disease states, and in the diagnosis of migraine and phaeochromocytoma.

The hazards of taking foods rich in tyramine while under treatment with MAOIs are described in the chapter on Antidepressants (see Phenelzine, p.417).

⊕ The bioavailability of tyramine given by mouth is significantly reduced by the presence of food, which could have implications when used in tyramine pressor tests.¹

1. VanDenBerg CM, *et al.* Tyramine pharmacokinetics and reduced bioavailability with food. *J Clin Pharmacol* 2003; **43**: 604-9.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: **Ger.:** Mydriol-Atropin†.

The symbol † denotes a preparation no longer actively marketed

Ubidecarenone (BAN, #INN)

Coenzyme Q10; Ubidecarenona; Ubidecarénone; Ubidecarenonum; Ubidekaronum; Ubidekarenonas; Ubidekaronum; Ubiquinone-10; 2-Deca(3-methylbut-2-enylene)-5,6-dimethoxy-3-methyl-*p*-benzoquinone.

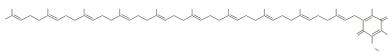
Убидекаренон

$C_{59}H_{90}O_4 = 863.3$.

CAS — 303-98-0.

ATC — C01EB09.

ATC Vet — QC01EB09.



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Jpn.*, and *US*.

Ph. Eur. 6.2 (Ubidecarenone). A yellow or orange crystalline powder. It gradually decomposes and darkens on exposure to light. M.p. about 48°. Practically insoluble in water; very slightly soluble in dehydrated alcohol; insoluble in acetone. Store in airtight containers. Protect from light.

USP 31 (Ubidecarenone). A yellow to orange, crystalline powder. M.p. about 48°. Practically insoluble in water; very slightly soluble in dehydrated alcohol; soluble in ether. Protect from light.

Profile

Ubidecarenone is a naturally occurring coenzyme involved in electron transport in the mitochondria. It is claimed to be a free radical scavenger and to have antioxidant and membrane stabilising properties. It has been given by mouth as an adjunct in cardiovascular disorders, including mild or moderate heart failure. It has also been tried in other conditions associated with coenzyme deficiency, and is promoted as a dietary supplement. Ubidecarenone is under investigation for the management of cancer, Huntington's chorea (p.953) and parkinsonism.

⊕ For discussion of the use of ubidecarenone in statin-induced muscle disorders, see Effects on Skeletal Muscle, under Simvastatin, p.1391.

References

- Greenberg S, Frishman WH. Co-enzyme Q : a new drug for cardiovascular disease. *J Clin Pharmacol* 1990; **30**: 596-608.
- Spigset O. Reduced effect of warfarin caused by ubidecarenone. *Lancet* 1994; **344**: 1372-3.
- Garcia Silva MT, *et al.* Improvement of refractory sideroblastic anaemia with ubidecarenone. *Lancet* 1994; **343**: 1039.
- Gattermann N, *et al.* No improvement of refractory sideroblastic anaemia with ubidecarenone. *Lancet* 1995; **345**: 1121-2.
- Nagao T, *et al.* Treatment of warfarin-induced hair loss with ubidecarenone. *Lancet* 1995; **346**: 1104-5.
- Pepping J. Coenzyme Q . *Am J Health-Syst Pharm* 1999; **56**: 519-21.
- Khatta M, *et al.* The effect of coenzyme Q in patients with congestive heart failure. *Ann Intern Med* 2000; **132**: 636-40.
- Tran MT, *et al.* Role of coenzyme Q10 in chronic heart failure, angina, and hypertension. *Pharmacotherapy* 2001; **21**: 797-806.
- Huntington Study Group. A randomized, placebo-controlled trial of coenzyme Q10 and remacemide in Huntington's disease. *Neurology* 2001; **57**: 397-404.
- Rahman S, *et al.* Neonatal presentation of coenzyme Q10 deficiency. *J Pediatr* 2001; **139**: 456-8.
- Roffe L, *et al.* Efficacy of coenzyme Q10 for improved tolerability of cancer treatments: a systematic review. *J Clin Oncol* 2004; **22**: 4418-24.
- Sándor PS, *et al.* Efficacy of coenzyme Q10 in migraine prophylaxis: a randomized controlled trial. *Neurology* 2005; **64**: 713-15.
- Levy HB, Kohlhaas HK. Considerations for supplementing with coenzyme Q during statin therapy. *Ann Pharmacother* 2006; **40**: 290-4.
- The NINDS NET-PD Investigators. A randomized clinical trial of coenzyme Q and GPI-1485 in early Parkinson disease. *Neurology* 2007; **68**: 20-8.
- Rosenfeldt FL, *et al.* Coenzyme Q in the treatment of hypertension: a meta-analysis of the clinical trials. *J Hum Hypertens* 2007; **21**: 297-306.

Preparations

USP 31: Ubidecarenone Capsules; Ubidecarenone Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: QX 100; **Braz.:** Coex†; Vinocard Q10; **Canad.:** Co-Q-10†; **Fr.:** Bio-Quinon Q10 Super†; Q10; **Hong Kong:** Co-Quinone†; Equinon; **Hung.:** Myoquinon; **Indon.:** Co-En Q; Ubi-Q; **Ital.:** Coedice†; Decafar; Decorenone; Iuvacor; Miodene†; Miotynt†; Mitocorr†; Oropigma Gel; Tricoxen; Ubicardio†; Ubicor; Ubidenone; Ubidec; Ubimaor; Ubiten†; Ubivis; **Jpn.:** Nequinon; **Malaysia:** Alerten; Bio-Quinone; Nequinon; **Philipp.:** Ad-dlife; Alerten; Nequinon; **Pol.:** Envit Q ; Vita Care Q ; **Port.:** Q 10; Ubenezima; Ubicondial†; **Singapore:** Co-Quinone; Ubi-Q; **Thai.:** Bio-Quinone; Decaquinon; **UK:** Co-Q-10†; **USA:** Co-Q-10†; Co-Quinone.

Multi-ingredient: **Arg.:** QX 10; **Canad.:** Mega AO; **Indon.:** Car-Q; Co-Q-10; Corsel; Lycoq; **RE-Q; Ital.:** Agedin Plus; Coquin; Ener-E†; Visu Q10; **Philipp.:** Immuvit; Nutrotal; **UK:** Red Kooga Co-Q-10 and Ginseng.

Ulinastatin (#INN)

Ulinastatina; Ulinastatine; Ulinastatinum; Urinastatin.

УлиНАСТАТИН

CAS — 80449-31-6; 80449-32-7.

Pharmacopoeias. In *Jpn.*

Profile

Ulinastatin is a glycoprotein proteolytic enzyme inhibitor isolated from human urine. It has been given by slow intravenous

injection or by intravenous infusion in acute pancreatitis (p.2361) and in acute circulatory insufficiency.

References

- Ohwada M, *et al.* New endoscopic treatment for chronic pancreatitis, using contrast media containing ulinastatin and prednisolone. *J Gastroenterol* 1997; **32**: 216-21.
- Sugita T, *et al.* Effect of a human urinary protease inhibitor (Ulinastatin) on respiratory function in pediatric patients undergoing cardiopulmonary bypass. *J Cardiovasc Surg* 2002; **43**: 437-40.
- Tsujino T, *et al.* Ulinastatin for pancreatitis after endoscopic retrograde cholangiopancreatography: a randomized, controlled trial. *Clin Gastroenterol Hepatol* 2005; **3**: 376-83.

Preparations

Proprietary Preparations (details are given in Part 3)

Jpn.: Miracilid.

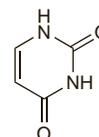
Uracil (USAN)

BMS-205603-01; Sq-6201; Sq-7726; Sq-8493. 2,4(1*H*,3*H*)-pyrimidinedione.

Урацил

$C_4H_4N_2O_2 = 112.1$.

CAS — 66-22-8.



Profile

Uracil is a pyrimidine base and one of the components of uridine nucleotides that form ribonucleic acid (p.2379). It inhibits dihydropyrimidine dehydrogenase and reduces the metabolism of fluorouracil; it is given orally with tegafur (p.776), an oral fluorouracil prodrug, to increase the bioavailability of fluorouracil.

Preparations

Proprietary Preparations (details are given in Part 3)

Cz.: UFT; **Thai.:** UFUR.

Multi-ingredient: **Arg.:** Asofural†; UFT; **Austria:** UFT; **Belg.:** UFT; **Braz.:** UFT; **Denm.:** Uftoral; **Fr.:** UFT; **Ger.:** UFT; **Gr.:** UFT; **Hong Kong:** UFT; **Hung.:** UFT; **Israe.:** UFT†; **Ital.:** UFT; **Jpn.:** UFT; **Malaysia:** UFT; **Mex.:** UFT; **Neth.:** UFT; **Norw.:** UFT; **NZ:** Orzel†; **Philipp.:** Tefudex; UFT; **Port.:** UFT; **Rus.:** UFT (УФТ); **S.Afr.:** UFT; **Singapore:** UFT; **Spain:** UFT; **Swed.:** UFT; **Thai.:** UFT; **Turk.:** UFT; **UK:** Uftoral.

Urazamide

5-Aminoimidazole-4-carboxamide ureidosuccinate.

$C_9H_{14}N_6O_6 = 302.2$.

Profile

Urazamide has been given orally in the treatment of hepatic disorders. It has also been given by intramuscular and intravenous injection.

Preparations

Proprietary Preparations (details are given in Part 3)

Ital.: Carbaic†.

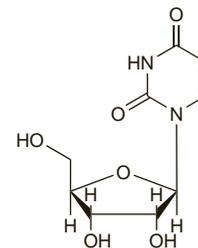
Uridine

Uracil Riboside; Uridina; Urydyna. 1-β-D-Ribofuranosyluracil; 1-β-D-Ribofuranosylpyrimidine-2,4(1*H*,3*H*)-dione.

УриДИН

$C_9H_{12}N_2O_6 = 244.2$.

CAS — 58-96-8.



Profile

Uridine is an endogenous uracil nucleoside involved in many biological processes; it is one of the components of nucleic acids (p.2355). Uridine is used in preparations containing other nucleosides in the treatment of corneal damage. It has been included in preparations for peripheral and cerebral vascular disorders and myopathies; it has also been used for liver disorders, anaemias,

The symbol ⊗ denotes a substance whose use may be restricted in certain sports (see p.vii)

and as a tonic. Uridine has been tried in patients with hereditary orotic aciduria.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: Belg.: Vitacic; Cz.: Laevadosin†; Hung.: Vitacit†; Ital.: Centrum; Mon.: Vitacic; Rus.: Vitacic (Витасик)†.

Uridine Triphosphate

Ins-316; Trifosfato de uridina; Uridina trifosfato; Uridine Triphosphoric Acid; UTP; Uridine 5'-(tetrahydrogen triphosphate).

Уридин Трифосфат

$C_9H_{15}N_2O_{13}P_3 = 484.1$.

ATC — G03-39-8.

Profile

Uridine triphosphate is an endogenous uracil nucleotide involved in many biological processes. It has been claimed to be of value in muscular atrophy and muscular weakness, and has been included in preparations for neuralgia, neuritis, and muscular disorders; the disodium and trisodium salts have also been used.

Uridine triphosphate has been reported to have beneficial effects on mucociliary clearance in chronic respiratory disease such as cystic fibrosis, asthma, and chronic bronchitis, although it may not be suitable for such therapy because it is rapidly degraded by enzymatic activity within sputum and by airway epithelial cells.^{1,2} It may, however, have a role as a method of producing deep-lung sputum specimens for cytological evaluation and is being investigated as an aid to the diagnosis of, for example, lung cancer^{1,2} or airway inflammation in asthma.³

- Bennett WD, *et al.* Effect of aerosolized uridine 5'-triphosphate on mucociliary clearance in mild chronic bronchitis. *Am J Respir Crit Care Med* 2001; **164**: 302-6.
- Johnson FL, *et al.* Improved sputum expectoration following a single dose of INS316 in patients with chronic bronchitis. *Chest* 2002; **122**: 2021-9.
- Tamaoki J, *et al.* Validity and safety of sputum induction by inhaled uridine 5'-triphosphate. *Am J Respir Crit Care Med* 2001; **164**: 378-81.

Preparations

Proprietary Preparations (details are given in Part 3)

Fr.: Uteplex; **Ital.:** Miocunil†.

Multi-ingredient: Arg.: Nucleo CMP†; Braz.: Nucleo CMP; Chile: Citoneuron; Ital.: Fosfotipi Vitaminico†; Mex.: Nucleo CMP; Spain: Cefabot; Nucleo CMP; Taurobeta†.

Ursodeoxycholic Acid (BAN, rINN)

Acide Ursodeoxycholique; Acide ursodéoxycholique; Ácido ursodeoxicolico; Acidum ursodeoxycholicum; Kyselina ursodeoxycholová; UDCA; Ursodeoksicholol rügestis; Ursodeoksikolik Asit; Ursodeokskoolihappo; Ursodeoxycholsyra; Ursodeoxycholic Acid; Ursodiol (USAN); Urzodezoxikólsav. 3 α ,7 β -Dihydroxy-5 β -cholan-24-oic acid.

Урсодезоксихолевая Кислота

$C_{24}H_{40}O_4 = 392.6$.

CAS — 128-13-2.

ATC — A05AA02.

ATC Vet — QA05AA02.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Jpn.*, and *US*.

Ph. Eur. 6.2 (Ursodeoxycholic Acid). A white or almost white powder. Practically insoluble in water and in dichloromethane; freely soluble in alcohol; slightly soluble in acetone.

USP 31 (Ursodiol). A white or almost white, crystalline powder. Practically insoluble in water; freely soluble in alcohol and in glacial acetic acid; sparingly soluble in chloroform; slightly soluble in ether. Store in airtight containers.

Stability. References.

- Mallett MS, *et al.* Stability of ursodiol 25 mg/mL in an extemporaneously prepared oral liquid. *Am J Health-Syst Pharm* 1997; **54**: 1401-4.
- Johnson CE, Streetman DD. Stability of oral suspensions of ursodiol made from tablets. *Am J Health-Syst Pharm* 2002; **59**: 361-3.

Adverse Effects and Precautions

Ursodeoxycholic acid may cause nausea, vomiting, and other gastrointestinal disturbances; diarrhoea is reported to occur less frequently than with chenodeoxycholic acid. Increased liver enzyme values are also less likely. Pruritus may occur. Treatment with ursodeoxycholic acid may cause more calcification of cholesterol stones than chenodeoxycholic acid.

Ursodeoxycholic acid should not be given to patients with intestinal and hepatic disorders that interfere with entero-hepatic circulation of bile salts (but see Chronic Liver Disease below). It is ineffective for the dissolution of calcified and pigment gallstones and is of no value in patients without a patent and functioning gallbladder. Licensed product information recommends that its use should be avoided in pregnancy.

References.

- Hempfling W, *et al.* Systematic review: ursodeoxycholic acid—adverse effects and drug interactions. *Aliment Pharmacol Ther* 2003; **18**: 963-72.

Interactions

Ursodeoxycholic acid should not be used with drugs that increase bile cholesterol such as oestrogenic hormones and cholesterol-lowering drugs such as clofibrate. Use with bile-acid binding drugs including antacids, charcoal, and colestyramine should be avoided since this may reduce the effectiveness of therapy with ursodeoxycholic acid.

For references to the possible effects of ursodeoxycholic acid on ciclosporin, see p.1828.

Pharmacokinetics

Ursodeoxycholic acid is absorbed from the gastrointestinal tract and undergoes enterohepatic recycling. It is partly conjugated in the liver before being excreted into the bile. Under the influence of intestinal bacteria the free and conjugated forms undergo 7 α -dehydroxylation to lithocholic acid, some of which is excreted directly in the faeces and the rest absorbed and mainly conjugated and sulfated by the liver before excretion in the faeces. However, in comparison with chenodeoxycholic acid, less ursodeoxycholic acid undergoes such bacterial degradation.

References.

- Crosignani A, *et al.* Clinical pharmacokinetics of therapeutic bile acids. *Clin Pharmacokinet* 1996; **30**: 333-58.

Uses and Administration

Ursodeoxycholic acid is a naturally occurring bile acid (see p.2266) present in small quantities in human bile. Ursodeoxycholic acid suppresses the synthesis and secretion of cholesterol by the liver and inhibits intestinal absorption of cholesterol. It is used for the dissolution of cholesterol-rich gallstones in patients with functioning gallbladders (see below). The licensed dose is 6 to 12 mg/kg daily as a single bedtime dose or in 2 or 3 divided doses; obese patients may require up to 15 mg/kg daily. The daily dose may be divided unequally and the larger dose given before bedtime to counteract the increase in biliary cholesterol concentration seen overnight. The time required for dissolution of gallstones is likely to be between 6 and 24 months depending on stone size and composition. Treatment should be continued for 3 to 4 months after radiological disappearance of the stones. A dose of 300 mg twice daily has been suggested for the prevention of gallstones in patients undergoing rapid weight loss. Ursodeoxycholic acid has also been given in reduced doses in combination with chenodeoxycholic acid (p.2280).

Ursodeoxycholic acid is also used in **primary biliary cirrhosis**. The usual dose is 10 to 15 mg/kg daily in 2 to 4 divided doses.

Ursodeoxycholic acid has been tried in the treatment of primary sclerosing cholangitis.

The more hydrophilic derivative, tauroursodeoxycholic acid, has also been used.

Chronic liver disease. The use of ursodeoxycholic acid in chronic liver diseases has been summarised.¹⁻⁵ There have been differing opinions of its value in primary biliary cirrhosis (below). Response has been reported in obstetric cholestasis of pregnancy.⁶⁻¹⁰ primary sclerosing cholangitis,¹¹ chronic active hepatitis,¹² and viral hepatitis.^{13,14} Although ursodeoxycholic acid is widely used in the treatment of obstetric cholestasis, data on its safety and efficacy in this indication are lacking, and its possible role therefore remains unclear until further larger studies have been done.¹⁵ See also Adverse Effects and Precautions, above. Ursodeoxycholic acid appears to be of benefit in liver disease associated with cystic fibrosis¹⁶⁻¹⁸ and in the UK the *BNFC* recommends a dose of 10 to 15 mg/kg twice daily in children and adolescents with this condition; alternatively the total daily dose may be given in 3 divided doses. Ursodeoxycholic acid had initially shown some promise in the treatment of nonalcoholic steatohepatitis,¹⁹ but a randomised, controlled study²⁰ failed to confirm this. There has also been some interest in the use of ursodeoxycholic acid to treat refractory graft-versus-host disease of the liver in transplant patients,²¹ and possibly as an adjuvant to immunosuppressant therapy²²⁻²⁴ after orthotopic liver transplantation (p.1815). It may also be of benefit in the prevention of hepatic complications following allogeneic bone marrow transplantation (p.1811).^{25,26} Ursodeoxycholic acid has shortened the clinical course of parenteral nutrition-associated cholestasis in very-low-birth-weight infants,²⁷ and the *BNFC* recommends a dose of 10 mg/kg three times daily for this purpose. Benefit has also been reported²⁸ in parenteral-nutrition associated cholestasis in children and adults, although the optimal timing and duration of therapy remains to be evaluated. Ursodeoxycholic acid has also been associated with a lower incidence of colonic dysplasia in patients with ulcerative colitis and primary sclerosing cholangitis.^{29,30} For sclerosing cholangitis in children and adolescents, the *BNFC* recommends a dose of 5 to 10 mg/kg 2 or 3 times daily up to a maximum of 15 mg/kg 3 times daily depending on response. In children with biliary atresia, ursodeoxycholic acid may be used to treat associated cholestasis. The *BNFC* suggests a dose of 5 mg/kg three times daily in neonates and children up to 2 years of age, the dose and frequency adjusted according to response up to a maximum of 10 mg/kg three times daily.

- de Caestecker JS, *et al.* Ursodeoxycholic acid in chronic liver disease. *Gut* 1991; **32**: 1061-5.
- Rubin RA, *et al.* Ursodiol for hepatobiliary disorders. *Ann Intern Med* 1994; **121**: 207-18.
- Kowdley KV. Ursodeoxycholic acid therapy in hepatobiliary disease. *Am J Med* 2000; **108**: 481-6.

- Trauner M, Graziadei IW. Review article: mechanisms of action and therapeutic applications of ursodeoxycholic acid in chronic liver diseases. *Aliment Pharmacol Ther* 1999; **13**: 979-95.
- Lazaridis KN, *et al.* Ursodeoxycholic acid: mechanisms of action and clinical use in hepatobiliary disorders. *J Hepatol* 2001; **35**: 134-46.
- Palma J, *et al.* Ursodeoxycholic acid in the treatment of cholestasis of pregnancy: a randomized, double-blind study controlled with placebo. *J Hepatol* 1997; **27**: 1022-8.
- Roncaglia N, *et al.* A randomised controlled trial of ursodeoxycholic acid and S-adenosyl-L-methionine in the treatment of gestational cholestasis. *Br J Obstet Gynaecol* 2004; **111**: 17-21.
- Kondrackiene J, *et al.* Efficacy and safety of ursodeoxycholic acid versus colestyramine in intrahepatic cholestasis of pregnancy. *Gastroenterology* 2005; **129**: 894-901.
- Glantz A, *et al.* Intrahepatic cholestasis of pregnancy: a randomized controlled trial comparing dexamethasone and ursodeoxycholic acid. *Hepatology* 2005; **42**: 1399-1405.
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- Lindor KD, *et al.* Ursodiol for primary sclerosing cholangitis. *N Engl J Med* 1997; **336**: 691-5.
- Rolandi E, *et al.* Effects of ursodeoxycholic acid (UDCA) on serum liver damage indices in patients with chronic active hepatitis: a double-blind controlled study. *Eur J Clin Pharmacol* 1991; **40**: 473-6.
- Puoti C, *et al.* Ursodeoxycholic acid and chronic hepatitis C infection. *Lancet* 1993; **341**: 1413-14.
- Angelico M, *et al.* Recombinant interferon- α and ursodeoxycholic acid versus interferon- α alone in the treatment of chronic hepatitis C: a randomized clinical trial with long-term follow-up. *Am J Gastroenterol* 1995; **90**: 263-9.
- Royal College of Obstetricians and Gynaecologists. Obstetric Cholestasis. RCOG Guideline No. 43 (issued January 2006). Available at: http://www.rcog.org.uk/resources/Public/pdf/obstetric_cholestasis43.pdf (accessed 01/07/08)
- Colombo C, *et al.* Effects of ursodeoxycholic acid therapy for liver disease associated with cystic fibrosis. *J Pediatr* 1990; **117**: 482-9.
- Cotting J, *et al.* Effects of ursodeoxycholic acid treatment on nutrition and liver function in patients with cystic fibrosis and longstanding cholestasis. *Gut* 1990; **31**: 918-21.
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PRIMARY BILIARY CIRRHOSIS. Primary biliary cirrhosis (PBC) is a chronic liver disease of unknown aetiology that develops due to progressive destruction of small and intermediate bile ducts within the liver, subsequently evolving to fibrosis and cirrhosis. Over 90% of patients are female, usually aged between 40 and 60 years. The disease is thought to be auto-immune in nature. Most patients develop antimitochondrial antibodies that may be evident even before disease is clinically apparent.^{1,2} Genetic factors and hormonal stimulation may play a role in precipitating PBC.^{1,2} Infectious agents such as *Chlamydia pneumoniae* (*Chlamydia pneumoniae*)³ or retroviruses⁴ may be involved in the pathogenesis.

Clinical manifestations include pruritus, fatigue, jaundice, hepatomegaly, and hypercholesterolaemia leading to xanthoma formation. In late disease portal hypertension, bleeding oesophageal varices and liver failure may develop. Impaired calcium and vitamin D absorption may result in osteomalacia or osteoporosis, and fat-soluble vitamin deficiencies may occur. There may be accumulation of copper in the liver.⁴ Other disorders including rheumatoid arthritis, scleroderma, thyroiditis, and Sjögren's syndrome may be associated with PBC.^{1,5}

The disease is slowly progressive, with a mean survival of 8 years for symptomatic patients, and 16 years for asymptomatic individuals.^{1,6} Despite its presumed auto-immune aetiology, few immunosuppressive drugs have shown any benefit,^{5,7} although newer drugs such as mycophenolate mofetil, sirolimus, and tacrolimus have yet to be fully evaluated.⁷