that half the usual dose should be used for those with a CC of less than 20 mL/minute per 1.73 m^2.

1. Malone RS, *et al.* Pharmacokinetics of levofloxacin and ciprofloxacin during continuous renal replacement therapy in critically ill patients. *Antimicrob Agents Chemother* 2001; **45:** 2949–54.

Inflammatory bowel disease. Ciprofloxacin has been given, sometimes with metronidazole, to treat active Crohn's disease[1,2] (see Inflammatory Bowel Disease, p.1697).

1. Prantera C, *et al.* An antibiotic regimen for the treatment of active Crohn's disease: a randomized, controlled clinical trial of metronidazole plus ciprofloxacin. *Am J Gastroenterol* 1996; **91:** 328–32.
2. Ishikawa T, *et al.* Metronidazole plus ciprofloxacin therapy for active Crohn's disease. *Intern Med* 2003; **42:** 318–21.

Tuberculosis. Reviews[1,2] of data obtained from controlled studies, cohorts, and case series, published up to March 2006, evaluating the clinical efficacy of fluoroquinolones for the treatment of tuberculosis (p.196) concluded that substituting or adding fluoroquinolones (in particular the older fluoroquinolones such as ciprofloxacin or ofloxacin) to established first-line treatment regimens did not confer additional benefits, although the newer fluoroquinolones are reported to have good *in-vitro* (levofloxacin, gatifloxacin, moxifloxacin) and *in-vivo* (gatifloxacin and moxifloxacin) bactericidal activity against *Mycobacterium tuberculosis*.[2]

There are very few controlled studies evaluating the use of fluoroquinolones in multi-drug resistant tuberculosis, but 2 retrospective studies support their effectiveness.[2] WHO guidelines[3,4] recommend that patients with multi-drug resistant tuberculosis and those who relapse after completing standard treatment regimens should receive second-line antituberculous drugs as part of a DOTS-plus regimen; such drugs do include ciprofloxacin and ofloxacin, as well as gatifloxacin, levofloxacin, and moxifloxacin. The usual recommended oral doses during the initial phase are as follows:

- ciprofloxacin: 1 to 1.5 g daily
- gatifloxacin: 400 mg daily
- moxifloxacin: 400 mg daily
- levofloxacin: 750 mg daily
- ofloxacin: 400 mg twice daily

1. Ziganshina LE, Squire SB. Fluoroquinolones for treating tuberculosis. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2008 (accessed 07/07/08).
2. Moadebi S, *et al.* Fluoroquinolones for the treatment of pulmonary tuberculosis. *Drugs* 2007; **67:** 2077–99.
3. WHO. *Treatment of tuberculosis: guidelines for national programmes*. 3rd ed. Geneva: WHO, 2003 (and 2004 revision). Available at: http://whqlibdoc.who.int/hq/2003/WHO_CDS_TB_2003.313_eng.pdf (accessed 24/01/07)
4. WHO. *Guidelines for the programmatic management of drug-resistant tuberculosis*. Geneva: WHO, 2006. Available at: http://whqlibdoc.who.int/publications/2006/9241546956_eng.pdf (accessed 03/03/08)

Preparations

BP 2008: Ciprofloxacin Intravenous Infusion; Ciprofloxacin Tablets; ***USP 31:*** Ciprofloxacin and Dexamethasone Otic Suspension; Ciprofloxacin Injection; Ciprofloxacin Ophthalmic Ointment; Ciprofloxacin Ophthalmic Solution; Ciprofloxacin Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Argeflox; Atibax C; Biotic; Blader†; Ciloxan; Cipro; Cipro-Otico; Ciprotenk; Cirflox-G; Ciriax; Crisacide; Exertial; Floraxina; Gino Ciriax; Golysine; Lorbifloxacina; Medaflox; Microsulf; Neflox; Novidat; Ocefax; Omaflaxina†; Plusgin†; Quisegen; Rexner; Septicide; Ultramicina; ***Austral.:*** C-Flox; Ciloquin; Ciloxan; Ciprol; Ciproxin; Profloxin; Proquin; ***Austria:*** Agyr†; Ciflox; Ciloxan; Cipromed; Ciprostad; Ciproxin; ***Belg.:*** Ciloxan; Ciprobel; Ciproxine; Docciproflo; ***Braz.:*** Bactoflox†; Biamotil; Ciflocina†; Ciflox; Cifloxan†; Cifloxtron; Ciloxan; Cinoflax; Ciprix; Cipro; Ciproant†; Ciprobiot†; Ciprocilin; Ciprocina†; Ciprodine; Ciprofar; Ciprofloxax†; Ciproflox†; Ciprofloxil; Cipromizin†; Cipronal†; Cipronom; Ciproxan†; Ciproxen; Ciproxil†; Ductocina; Floxan; Maxiflox; Nixin; Ofoxin; Procin†; Proflox; Proxacin; Quiflox; Quinoflox; Sifloxan†; ***Canad.:*** Ciloxan; Cipro; ***Chile:*** Baycip; Ciflоxin; Ciloxacin; Ciproval; Ciproxino; Grifociprox; Oflono; Oftaciprox; ***Cz.:*** Cifloxinal; Cifran; Ciloxan; Ciphin; Ciplox; Ciprinol; Ciprobay; Ciprobid†; Ciprum; Quintor†; Quipro†; ***Denm.:*** Cifin; Ciloxan; Ciproxin; Sancipro; Sibunar; ***Fin.:*** Cipromed; Ciproxin; Siprion†; ***Fr.:*** Ciflox; Ciloxan; Uniflox; ***Ger.:*** Ciloxan; Cipro; Cipro-Lich†; Cipro-Q; Cipro-saar; Cipro-Wolff; Ciprobay; Ciprobeta; Ciprodoc; Ciprodura; Ciprofat; Ciproflox; Ciproflox-Puren; Ciprogamma; Ciprohexal; Ciprox; Gyracip; Keciflox; Panotile cipro; ***Gr.:*** Afenoxin; Aristin-C; Balepton; Biocipro; Bivorilan; Cidrops†; Ciloxan; Ciprobay†; Ciprofal; Cipromycin; Ciprospes; Ciproxin; Citrovenot; Droll; Flociprin; Forterra; Ginorectol; Glossyfin; Grenis-cipro; Infectina; Labentrol; Ladinin; Limox; Nafloxin; Ravalton; Remena; Revion; Revionorm; Topistin; Ufexil; Urodixin; ***Hong Kong:*** Ciflоxin; Ciloxan; Cipide; Ciplox; Ciprol; Ciproxin; Ciproxyl; Cyfloxin; Enoxin; Gonning; Medociprin; Proxacin; Quinocin; Uroxin; Utahzone; ***Hung.:*** Ciflоxin; Cifran; Ciloxan; Ciphin; Ciplox; Ciprinol; Ciprobay; Ciprolen; Cipropharm; Ciprum; Cydonin; ***India:*** Bactoquin†; Biocip; Cifran; Cipgen; Cipro-Cent; Ciprobid; Ciprodac; Ciprowin; Ificipro†; Neocip; Procip†; Quinobact; Strox†; Zoxan; ***Indon.:*** Bactiprox; Baquinor; Bernoflox; Bidiprox; Cetafloxo; Ciflos; Cilox; Ciproxin; Civell; Coroflex; Corsacin; Cylowam; Disfabac; Duflomex; Etacin; Floksid; Floxbio; Floxigra; Girabloc; Interflox; Isotic Renator; Jayacin; Kifarox; Lapiflox; Licoprox; Meflosin; Mensipox; Nilaflox; Poncoflox; Proxcip; Proxitor; Qinox; Quamiprox; Quidex; Quinobiotic; Renator; Scanax; Tequinol; Vidintal; Viflox; Vioquin; Volinol; Wiaflox; Ximex Cylowam; Zumaflox; ***Irl.:*** Biofloxcin; Cifloxager; Ciproxin; Profloxin; Truoxin; ***Israel:*** Ciloxan; Ciplox; Ciprodex; Ciprogis; Ciproxin; Ufexil; ***Ital.:*** Ciproxin; Flociprin; Oftacilox; ***Jpn:*** Ciproxan; ***Malaysia:*** Bactiflox; Cifloxin; Cifran; Ciloxan; Ciprobay; Enoxin; ***Mex.:*** Antimed; Apoflox; Arfloxina; Bacproin; Bioflox; Ci-Sons; Cifran; Ciloxan; Cimogal; Ciprain; Cipro; Ciprobac; Ciprobiotic; Ciproflox; Ciprofur; Ciprohexal; Ciproser; Ciprotec; Ciproxina; Ciqfadin; Dinaflox; Eni; Eufloxin; Floxager; Floxantina; Floxelena; Floxitul; Gibac; Infloxa; Italnik; Kenzoflex; Lemyflox; Lifexina; Maviflox†; Microrgan; Mitroken; Nivoflox†; Novoquin; Oftaquin†; Opthaflox; Patox; Pharcina; Profluxol; Provay; Proxitec†; Quifloxona†; Quinoflox; Rictor; Sinfexina; Sophixin; Spectroflex†; Suiflox; Trigen; Vifloxina; Zipra; ***Neth.:*** Ciloxan; Ciprinol; Ciproxin; ***Norw.:*** Cilox; Ciproxin; ***NZ:*** Cifran; Ciloxan; Cipflox; Ciproxin; DP-Cipro; Topistin; Ufexil; ***Philipp.:*** Baxolyn; Brelcip; Ciclodin; Cidroxal; Ciloxan; Ciprobay; Cipromax; Cipromet; Ciprotor; Cirok; Floroc; Iprolan; Ipromax; Kinoves; Laitun; Nexproxyn; Proxivex; Qinosyn; Quilox; Quinoryl; Quiprime; Rapiqure; Xipro; Zalvos; Zyflox; ***Pol.:*** Cifran; Ciloxan; Ciphin; Ciprinol; Ciprobay; Cipronex; Ciropol; Ciprum; Proxacin; ***Port.:*** Carmicina†; Ciflan; Ciplox; Ciproquinol†; Ciproxina; Colintil; Estecina; Floxacipront†; Giroflox; ISINO; Keefloxin†; Megaflox; Nivoflox; Nixin; Oftacilox; Quinox; Xorpic†; ***Rus.:*** Ciflоxinal (Ципрофлоксинал); Cifran (Ципран); Ciloxan (Цилоксан); Ciprex (Ципрекс); Ciprinol (Ципринол); Ciprobay (Ципробай); Ciprobid (Ципробид); Ciprolet (Ципролет); Ciprolone (Ципролон); Cipromed (Ципромед); Ciprosun (Ципросан); Ificipro (Ифиципро); Medociprin (Медоциприн); Quintor (Квинтор); Sifloks (Сифлокс); ***S.Afr.:*** Adco-Ciprin; Biocip; Cifloc; Cifran; Ciloxan; Ciploxx; Cipro-Hexal; Ciprobay; Ciprogen; Dynafloc; Orpic; Spec-Topistin; ***Singapore:*** Ciloxan; Ciprobay; Ciprolet; Cirok†; Ciroxin†; Cycin; Ginorectol; Neofloxin; Serviflox; Uroxin; ***Spain:*** Aceoto; Baycip; Belmacina; Catex; Ceprimax†; Cetraxal; Cipobacter†; Ciprenit Otico; Ciproctal; Ciproxina Simple; Cunesin; Doriman; Estecina; Felixene; Giroflox; Globuce; Huberdoxina; Numen; Oftacilox; Otociprin; Otosat; Piprol; Plenolyt; Quipro; Rigoran; Sepcen; Septocipro; Tam; Ultramicina; Velmonit†; ***Swed.:*** Ciloxan; Ciproxin; ***Switz.:*** Ciloxan; Cip eco; Ciprine; Cipro-Med; Ciproflox; Ciproxine; Principrox; ***Thai.:*** C-Floxacin; Ciflo; Ciflolan; Cifloxin; Cifran; Cilab; Ciloxan; Cinfloxine; Cipflocin; Cipon; Ciprobay; Ciprobid; Ciprocep; Ciprofin; Ciprogen; Ciproglen†; Ciprolet; Ciprom-H; Ciprosun†; Ciprovid; Ciproxan; Ciproxyl; Cobay; Cyflox; Forexin; Microflox; Poli-Cifloxin; Proflox; Serviflox†; Ultraflox; Uroxin; Vesprocin; ***Turk.:*** Ciflosin; Cifluron; Ciloxan; Ciprasid; Cipro; Ciproktan; Ciproxin; Loxasid; Proxacin; Roflazin; Roxin; Sanset; Sifloks; Siprobel; Siprogut; Siprosan; Sispres; UroCiproxin; ***UAE:*** Sarf; ***UK:*** Ciloxan; Ciproxin; ***USA:*** Ciloxan; Cipro; ***Venez.:*** Bacipro; Baflox; Ciflox; Ciloxan; Ciprivax; Ciproflox; Ciprolet†; Cipronax; Ciproquin; Ciproxina; Cirok; Cypral; Gerxidin†; Iproxin; Klicina†; Lisipin; Oxtin; Quinoftal; Quinotic; Serviflox; Sophixin; Zolina.

Multi-ingredient: ***Arg.:*** Ciloxadex; Cipro HC; Ciproflox-Otic; Ciriax Otic; Ciriax Otic L; Decadron con Ciprofloxina; Delos Otic; Otex HC; Oto Biotaer; Otobiotic; Otocipro; Otosporin C; Prootocipro; Quidex; Tacines; ***Austral.:*** Ciproxin HC; ***Austria:*** C-Bildz; ***Braz.:*** Biamotil-D; Cilodex; Cipro HC; Cylocort; Maxiflox D; Otociriax; ***Canad.:*** Cipro HC; Ciprodex; ***Chile:*** Cilodex; Ciprodex; Oflono-D; Otex HC; ***Cz.:*** Ciprobay HC Otic; ***Denm.:*** Ciflox; ***Fin.:*** Ciproxin-Hydrocortison; ***Gr.:*** Ciprofloxacin HY†; ***Hong Kong:*** Cipro HC; ***Hung.:*** Ciprobay†; ***India:*** Biocip-TZ; Cipgen TZ; Ciplox; Ciplox D; Ciplox TZ; Ciptini; Citizol; Neocip FC; Neocip M; Ocimix; Tinvista-CF; ***Israel:*** Ciproxin HC; ***Malaysia:*** Cipro HC†; ***Mex.:*** Cilodex; Ciproxina HC; Dinill-D; Oto Eni; Quinoflox Otico; UV IX†; Vodelan; ***NZ:*** Ciproxin HC; ***S.Afr.:*** Ciprobay HC; ***Singapore:*** Ciprobay HC; ***Spain:*** Aceoto Plus; Cetraxal Plus; Cexidal Otico†; Ciproxina; Synalotic; Ultramicina Plus†; ***Switz.:*** Ciproxin HC; ***USA:*** Cipro HC; Ciprodex; ***Venez.:*** Otalex; Quinocort; Quinotic HC.

Clarithromycin *(BAN, USAN, rINN)*

A-56268; Abbott-56268; Clarithromycine; Clarithromycinum; Claritromicina; Klarithromycin; Klaritromicinas; Klaritromisin; Klaritromycin; Klaritromysiini; TE-031. (2*R*,3*S*,4*S*,5*R*,6*R*,8*R*,10*R*,11*R*,12*S*,13*R*)-3-(2,6-Dideoxy-3-*C*,3*O*-dimethyl-α-L-*ribo*-hexopyranosyloxy)-11,12-dihydroxy-6-methoxy-2,4,6,8,10,12-hexamethyl-9-oxo-5-(3,4,6-trideoxy-3-dimethylamino-β-D-*xylo*-hexopyranosyloxy)pentadecan-13-olide; 6-*O*-Methylerythromycin.

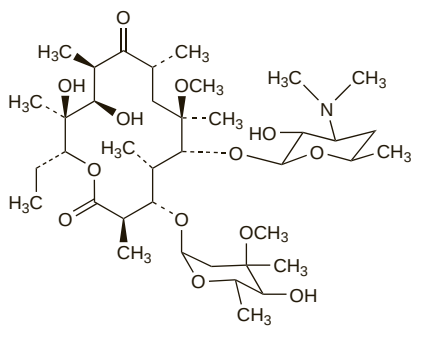
Кларитромицин

$C_{38}H_{69}NO_{13}$ = 748.0.

CAS — 81103-11-9.

ATC — J01FA09.

ATC Vet — QJ01FA09.



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

Ph. Eur. 6.2 (Clarithromycin). A white or almost white, crystalline powder. Practically insoluble in water; soluble in acetone and in dichloromethane; slightly soluble in methyl alcohol.

USP 31 (Clarithromycin). A white to off-white crystalline powder. Practically insoluble in water; slightly soluble in dehydrated alcohol, in methyl alcohol, and in acetonitrile; soluble in acetone; slightly soluble in phosphate buffer at pH values of 2 to 5. pH of a 0.2% suspension in a mixture of water and methyl alcohol (19:1) is between 8.0 and 10.0. Store in airtight containers.

Adverse Effects and Precautions

As for Erythromycin, p.270. Gastrointestinal disturbances are the most frequent adverse effect but are usually mild and less frequent with clarithromycin than with erythromycin. Smell and taste disturbances, stomatitis, glossitis, tongue and tooth discoloration, and headache have occurred. There have also been reports of transient CNS effects. Other adverse effects include arthralgia, myalgia, hypoglycaemia, leucopenia, and thrombocytopenia. Interstitial nephritis and renal failure have been reported rarely.

Intravenous doses may cause phlebitis and pain at the injection site.

Caution is required in patients with hepatic or renal impairment and doses should be reduced in those with renal impairment (see under Uses and Administration below). It should not be used during pregnancy if possible as high doses have been associated with embryotoxicity in *animal* studies.

Effects on the blood. Single cases of thrombocytopenia[1] and thrombocytopenic purpura[2,3] associated with clarithromycin have been reported. Cases of agranulocytosis have also been reported.[4] A case of thrombocytopenia accompanied by interstitial nephritis, hepatitis, and elevated serum amylase levels was attributed to an allergic reaction to clarithromycin.[5] Toxic epidermal necrolysis and subsequent death due to aplastic anaemia have been reported in a patient after taking clarithromycin for 3 days.[6]

1. Price TA, Tuazon CU. Clarithromycin-induced thrombocytopenia. *Clin Infect Dis* 1992; **15:** 563–4.
2. Oteo JA, *et al.* Clarithromycin-induced thrombocytopenic purpura. *Clin Infect Dis* 1994; **19:** 1170–1.
3. Alexopoulou A, *et al.* Thrombotic thrombocytopenic purpura in a patient treated with clarithromycin. *Eur J Haematol* 2002; **69:** 191–2.
4. Jacobs P, *et al.* Immune agranulocytosis and clarithromycin. *Hematology* 2004; **9:** 291–6.
5. Baylor P, Williams K. Interstitial nephritis, thrombocytopenia, hepatitis, and elevated serum amylase levels in a patient receiving clarithromycin therapy. *Clin Infect Dis* 1999; **29:** 1350–1.
6. Baz K, *et al.* Fatal aplastic anaemia in a patient with clarithromycin-induced toxic epidermal necrolysis. *J Eur Acad Dermatol Venereol* 2004; **18:** 104–5.

Effects on the cardiovascular system. QT prolongation and torsade de pointes were associated with use of clarithromycin in 2 patients.[1] Renal impairment in 1 of the patients and hepatic impairment and organic heart disease in both could have increased their susceptibility to these effects.

For mention of an unexpected increase in cardiovascular mortality in patients with stable coronary heart disease given clarithromycin, see Ischaemic Heart Disease, in Uses and Administration of Azithromycin, above.

1. Lee KL, *et al.* QT prolongation and torsades de pointes associated with clarithromycin. *Am J Med* 1998; **104:** 395–6.

Effects on the eyes. Corneal opacities, reversible on stopping treatment, were reported in a patient receiving oral clarithromycin as part of a regimen for disseminated *Mycobacterium avium* complex infection.[1] Corneal subepithelial deposits have also been reported in a patient after prolonged use of clarithromycin eye drops for *Mycobacterium avium* complex keratitis. The deposits did not cause any ocular discomfort and resolved on stopping therapy.[2]

1. Dorrell L, *et al.* Toxicity of clarithromycin in the treatment of Mycobacterium avium complex infection in a patient with AIDS. *J Antimicrob Chemother* 1994; **34:** 605–6.
2. Tyagi AK, *et al.* An unreported side effect of topical clarithromycin when used successfully to treat Mycobacterium avium-intracellulare keratitis. *Cornea* 1999; **18:** 606–7.

Effects on the gastrointestinal tract. Pseudomembranous colitis associated with *Clostridium difficile* developed in a child receiving clarithromycin.[1]

1. Braegger CP, Nadal D. Clarithromycin and pseudomembranous enterocolitis. *Lancet* 1994; **343:** 241–2.

Effects on the liver. Progressive cholestatic jaundice, which subsequently proved fatal, developed in a 59-year-old woman after 3 days of clarithromycin therapy for acute maxillary sinusitis.[1] Fulminant hepatic failure in another patient, which developed during clarithromycin therapy, resolved once the drug was withdrawn.[2] Clarithromycin itself was considered responsible although there was the possibility that it had increased concentrations of isradipine, another known hepatotoxic drug that the patient was also receiving.

1. Fox JC, *et al.* Progressive cholestatic liver disease associated with clarithromycin treatment. *J Clin Pharmacol* 2002; **42:** 676–80.
2. Tietz A, *et al.* Fulminant liver failure associated with clarithromycin. *Ann Pharmacother* 2003; **37:** 57–60.

Effects on the lungs. On 2 occasions fever and pulmonary infiltration with eosinophilia occurred in a patient given clarithromycin.[1] Another patient developed eosinophilic pneumonia 3 days after starting clarithromycin; symptoms improved when the drug was stopped.[2]

1. Terzano C, Petroianni A. Clarithromycin and pulmonary infiltration with eosinophilia. *BMJ* 2003; **326:** 1377–8.
2. Ohnishi H, *et al.* Clarithromycin-induced eosinophilic pneumonia. *Intern Med* 2004; **43:** 231–5.

Effects on mental state. Acute psychoses occurred in 2 patients receiving clarithromycin as part of prophylactic treatment for *Helicobacter pylori* infection and were similar to 3 previous-

ly reported cases in either AIDS patients or elderly subjects.[1] Delirium[2] has also been associated with clarithromycin monotherapy in an elderly patient, and visual hallucinations have occurred in a 37-year-old woman being treated with ceftriaxone and clarithromycin for suspected pneumonia.[3] A review[4] of published and spontaneous reports found an association between adverse manic reactions and the use of certain antibacterials; clarithromycin was found to be the antibacterial most frequently implicated.

1. Gómez-Gil E, *et al.* Clarithromycin-induced acute psychoses in peptic ulcer disease. *Eur J Clin Microbiol Infect Dis* 1999; **18:** 70–1.
2. Özsoylar G, *et al.* Clarithromycin monotherapy-induced delirium. *J Antimicrob Chemother* 2007; **59:** 331.
3. Fernández Arenas O, *et al.* Alucinaciones por administración de una pauta estándar de claritromicina. *Farm Hosp* 2007; **31:** 315–16.
4. Abouesh A, *et al.* Antimicrobial-induced mania (antibiomania): a review of spontaneous reports. *J Clin Psychopharmacol* 2002; **22:** 71–81.

Effects on the pancreas. Pancreatitis has been reported in patients receiving clarithromycin.[1-3]

1. Liviu L, *et al.* Pancreatitis induced by clarithromycin. *Ann Intern Med* 1996; **125:** 701.
2. Schouwenberg BJJW, Deinum J. Acute pancreatitis after a course of clarithromycin. *Neth J Med* 2003; **61:** 266–7.
3. González Carro P, *et al.* Acute pancreatitis and modified-release clarithromycin. *Ann Pharmacother* 2004; **38:** 508–509.

Hypersensitivity. In addition to skin rashes and other hypersensitivity reactions which occasionally occur in patients receiving macrolides, leukocytoclastic vasculitis,[1] Henoch-Schönlein purpura,[2] and toxic epidermal necrolysis[3] have been reported in patients receiving clarithromycin.

1. Gavura SR, Nusinowitz S. Leukocytoclastic vasculitis associated with clarithromycin. *Ann Pharmacother* 1998; **32:** 543–5.
2. Borrás-Blasco J, *et al.* Henoch-Schönlein purpura associated with clarithromycin: case report and review of literature. *Int J Clin Pharmacol Ther* 2003; **41:** 213–16. Correction. *ibid.*; 420.
3. Khaldi N, *et al.* Toxic epidermal necrolysis and clarithromycin. *Can J Clin Pharmacol* 2005; **12:** e264–e268.

Interactions

For a discussion of drug interactions of macrolide antibacterials, see Erythromycin, p.271.

Antidiabetics. For reference to hypoglycaemia resulting from the addition of clarithromycin to *glibenclamide* or *glipizide*, see Antibacterials, p.462.

Antiretroviral drugs. In studies in healthy subjects,[1,2] the HIV-protease inhibitor *ritonavir* inhibited the metabolism of clarithromycin, increasing plasma concentrations and prolonging half-life. The metabolism of ritonavir was not affected significantly. The two drugs may be given together in usual doses to those with normal renal function but licensed product information for clarithromycin recommends that its dose should be reduced in patients with renal impairment receiving ritonavir and it should be noted that this is an extra reduction over and above that which may be needed for the renal impairment alone. Doses of clarithromycin should be reduced by 50% in patients with a creatinine clearance (CC) of 30 to 60 mL/minute and reduced by 75% in those with a CC below 30 mL/minute; the daily dose should not exceed 1 g. It has been suggested that other HIV-protease inhibitors (see also Table of Interactions of Drugs Used in the Treatment of HIV, p.917) and the NNRTI *delavirdine* may have a similar effect on clarithromycin. Use of *efavirenz* with clarithromycin has decreased plasma concentration of clarithromycin and increased its hydroxy metabolite. The combination has been associated with a high incidence of skin rashes. Decreases in the plasma concentration of clarithromycin have also been noted with *nevirapine*.

Decreased concentrations of *zidovudine* (p.915) have been reported in patients also taking clarithromycin and clarithromycin product information recommends that doses of the two drugs should be separated by 1 to 2 hours.

1. Ouellet D, *et al.* Assessment of the pharmacokinetic interaction between ritonavir and clarithromycin. *Clin Pharmacol Ther* 1996; **59:** 143.
2. Ouellet D, *et al.* Pharmacokinetic interaction between ritonavir and clarithromycin. *Clin Pharmacol Ther* 1998; **64:** 355–62.

Colchicine. For mention of fatal colchicine toxicity associated with concomitant use of clarithromycin, see Macrolides, p.557.

Disulfiram. For a report of an interaction between clarithromycin and disulfiram, see Macrolides, p.2297.

Fluoxetine. For a report of delirium following use of clarithromycin with fluoxetine, see Antibacterials, p.396.

Gastrointestinal drugs. In a study[1] in healthy subjects, concentrations of clarithromycin and its active metabolite were increased in gastric tissue and mucus and, to a lesser extent, in plasma during use of *omeprazole*. In addition, use of clarithromycin with omeprazole resulted in higher and more prolonged plasma concentrations of omeprazole. The investigators suggest that this interaction could account for the synergistic action observed with this combination when used for eradication of *Helicobacter pylori*. However, licensed product information for clarithromycin states that no dosage adjustment to either drug is necessary.

Although a study[2] in healthy subjects suggested that some pharmacokinetic parameters of clarithromycin are altered by *cimetidine*, the clinical significance of such changes are unknown.

1. Gustavson LE, *et al.* Effect of omeprazole on concentrations of clarithromycin in plasma and gastric tissue at steady state. *Antimicrob Agents Chemother* 1995; **39:** 2078–83.
2. Amsden GW, *et al.* Oral cimetidine prolongs clarithromycin absorption. *Antimicrob Agents Chemother* 1998; **42:** 1578–80.

Antimicrobial Action

As for Erythromycin, p.271.

Clarithromycin is reported to be more active than erythromycin against susceptible streptococci and staphylococci *in vitro*, as well as against some other species including *Moraxella catarrhalis* (*Branhamella catarrhalis*), *Legionella* spp., *Chlamydia trachomatis*, and *Ureaplasma urealyticum*. Clarithromycin is reported to be more active than erythromycin or azithromycin against some mycobacteria, including *Mycobacterium avium* complex and *M. leprae*. It is reported to have some *in-vitro* activity against the protozoan *Toxoplasma gondii*. The major metabolite, 14-hydroxyclarithromycin, is also active, and may enhance the activity of clarithromycin *in vivo*, notably against *Haemophilus influenzae*. The MICs of this metabolite are equal or twofold higher than those of the parent drug; the former is twofold more active than the latter against *H. influenzae*.

Activity with other antimicrobials. Clarithromycin has been reported to enhance the activity of a number of antimycobacterials including ethambutol, isoniazid, pyrazinamide, and rifampicin against *Mycobacterium tuberculosis*.[1,2]

1. Cavalieri SJ, *et al.* Synergistic activities of clarithromycin and antituberculous drugs against multi drug-resistant Mycobacterium tuberculosis. *Antimicrob Agents Chemother* 1995; **39:** 1542–5.
2. Mor N, Esfandiari A. Synergistic activities of clarithromycin and pyrazinamide against Mycobacterium tuberculosis in human macrophages. *Antimicrob Agents Chemother* 1997; **41:** 2035–6.

Resistance. Erythromycin-resistant isolates of *Streptococcus pneumoniae* are commonly cross-resistant to clarithromycin.[1] The incidence of resistance to clarithromycin and other macrolides is higher among penicillin-resistant strains than among penicillin-sensitive strains.[2] Clarithromycin-resistant isolates of *Helicobacter pylori* have also emerged.[3-6] Genetic mutations responsible for clarithromycin resistance have been identified in *H. pylori*[7] and in *Mycobacterium* spp.[8,9] Since resistance develops rapidly in *M. avium* during clarithromycin monotherapy, combination therapy is usually recommended. However, resistance to clarithromycin in an AIDS patient with systemic *M. avium* complex infection, despite combined treatment with clofazimine, has been described.[10]

1. Lonks JR, Medeiros AA. High rate of erythromycin and clarithromycin resistance among Streptococcus pneumoniae isolates from blood cultures from Providence, RI. *Antimicrob Agents Chemother* 1993; **37:** 1742–5.
2. Barry AL, *et al.* Macrolide resistance among Streptococcus pneumoniae and Streptococcus pyogenes isolates from out-patients in the USA. *J Antimicrob Chemother* 1997; **40:** 139–40.
3. López-Brea M, *et al.* Evolution of resistance to metronidazole and clarithromycin in Helicobacter pylori clinical isolates from Spain. *J Antimicrob Chemother* 1997; **40:** 279–81.
4. Hultén K, *et al.* Macrolide resistance in Helicobacter pylori: mechanism and stability in strains from clarithromycin-treated patients. *Antimicrob Agents Chemother* 1997; **41:** 2550–3.
5. Kalach N, *et al.* High levels of resistance to metronidazole and clarithromycin in Helicobacter pylori strains in children. *J Clin Microbiol* 2001; **39:** 394–7.
6. Grove DI, Koutsouridis G. Increasing resistance of Helicobacter pylori to clarithromycin: is the horse bolting? *Pathology* 2002; **34:** 71–3.
7. Versalovic J, *et al.* Mutations in 23S rRNA are associated with clarithromycin resistance in Helicobacter pylori. *Antimicrob Agents Chemother* 1996; **40:** 477–80.
8. Nash KA, Inderlied CB. Genetic basis of macrolide resistance in Mycobacterium avium isolated from patients with disseminated disease. *Antimicrob Agents Chemother* 1995; **39:** 2625–30.
9. Wallace RJ, *et al.* Genetic basis for clarithromycin resistance among isolates of Mycobacterium chelonae and Mycobacterium abscessus. *Antimicrob Agents Chemother* 1996; **40:** 1676–81.
10. De Wit S, *et al.* Acquired resistance to clarithromycin as combined therapy in Mycobacterium avium intracellulare infection. *Lancet* 1993; **341:** 53–4.

Pharmacokinetics

Clarithromycin is rapidly absorbed from the gastrointestinal tract, and undergoes first-pass metabolism; the bioavailability of the parent drug is about 55%. The extent of absorption is relatively unaffected by the presence of food. Peak plasma concentrations occur 2 to 3 hours after an oral dose. At steady state, peak plasma concentrations of clarithromycin and its principal active metabolite, 14-hydroxyclarithromycin, are about 1 and 0.6 micrograms/mL, respectively, after 250 mg orally every 12 hours as tablets. The same dose given as a suspension to fasting subjects produces steady-state plasma concentrations of about 2 micrograms/mL of clarithromycin and about 0.7 micrograms/mL of 14-hydroxyclarithromycin. Steady-state concentrations are reached within 3 to 4 days.

The pharmacokinetics of clarithromycin are non-linear and dose dependent; high doses may produce disproportionate increases in peak concentrations of the parent drug, due to saturation of the metabolic pathways. However, the non-linearity is slight at the recommended doses of 250 to 500 mg every 8 to 12 hours.

Clarithromycin and 14-hydroxyclarithromycin are widely distributed, and tissue concentrations exceed those in serum, in part because of intracellular uptake. Plasma protein binding has been reported to be about 80%. Clarithromycin has been detected in breast milk. It is extensively metabolised in the liver, and excreted in faeces via the bile; 5 to 10% of the parent drug is recovered from the faeces. At steady state, about 20% and 30% of a 250-mg or 500-mg dose as tablets, respectively, and about 40% of a 250-mg dose as suspension, is excreted in the urine as unchanged drug. 14-Hydroxyclarithromycin as well as other metabolites are also excreted in the urine, accounting for 10 to 15% of the dose. The elimination half-lives of clarithromycin and 14-hydroxyclarithromycin are about 3 to 4 and 5 to 6 hours, respectively in patients receiving 250 mg every 12 hours, and about 5 to 7 and 7 to 9 hours, respectively, in those receiving 500 mg every 8 to 12 hours. The half-life is prolonged in renal impairment.

◊ Reviews.

1. Rodvold KA. Clinical pharmacokinetics of clarithromycin. *Clin Pharmacokinet* 1999; **37:** 385–98.

Uses and Administration

Clarithromycin is a macrolide derived from erythromycin with similar actions and uses (p.272). It is given in the treatment of respiratory-tract infections (including otitis media) and in skin and soft-tissue infections. Clarithromycin is also used for the prophylaxis and treatment of nontuberculous mycobacterial infections and has been used as a second-line drug in the treatment of leprosy. It is used in some countries as an alternative to penicillins for prophylaxis of endocarditis.

For details of all these infections and their treatment, see under Choice of Antibacterial, p.162.

Clarithromycin may be given to eradicate *Helicobacter pylori* in treatment regimens for peptic ulcer disease (p.1702). It is used with pyrimethamine as an alternative regimen in the treatment of toxoplasmosis (p.826).

Clarithromycin is given orally or by intravenous infusion. Some clarithromycin preparations are prepared with the aid of lactobionic acid and may be stated to contain clarithromycin lactobionate. Doses are expressed in terms of the equivalent amount of clarithromycin.

Usual oral doses in adults are 250 mg twice daily, increased to 500 mg twice daily if necessary in severe infection. Modified-release tablets allowing once-daily use are available in some countries.

The usual intravenous dose is 500 mg twice daily, given as an infusion over 60 minutes using a solution containing about 0.2% of clarithromycin. Intravenous treatment may continue for 2 to 5 days, but should be changed to oral clarithromycin when possible.

For treatment and prophylaxis of disseminated infection due to *Mycobacterium avium* complex, clarithromycin may be given in an oral dose of 500 mg twice daily; for treatment, it should be given with other antimycobacterials. For leprosy, oral clarithromycin 500 mg daily has been given as part of an alternative multidrug therapy regimen.

For the eradication of *H. pylori* associated with peptic ulcer disease, clarithromycin, usually in an oral dose of 500 mg twice daily, is given with another antibacterial

and either a proton pump inhibitor or a histamine H_2-receptor antagonist, for 7 to 14 days.

For details of doses in infants and children, see below.

Doses may need to be reduced in patients with severe renal impairment (see below).

◊ Reviews.

1. Peters DH, Clissold SP. Clarithromycin: a review of its antimicrobial activity, pharmacokinetic properties and therapeutic potential. *Drugs* 1992; **44:** 117–64.
2. Barradell LB, *et al.* Clarithromycin: a review of its pharmacological properties and therapeutic use in Mycobacterium avium-intracellulare complex infection in patients with acquired immune deficiency syndrome. *Drugs* 1993; **46:** 289–312.
3. Markham A, McTavish D. Clarithromycin and omeprazole: as Helicobacter pylori eradication therapy in patients with H. pylori-associated gastric disorders. *Drugs* 1996; **51:** 161–78.
4. Alvarez-Elcoro S, Enzler MJ. The macrolides: erythromycin, clarithromycin, and azithromycin. *Mayo Clin Proc* 1999; **74:** 613–34.
5. Zuckerman JM. Macrolides and ketolides: azithromycin, clarithromycin, telithromycin. *Infect Dis Clin North Am* 2004; **18:** 621–49.

Administration in children. The usual oral dose of clarithromycin for infants and children is 7.5 mg/kg twice daily; those over 12 years of age may be given the usual adult dose (see above).

Although intravenous use is not licensed for children in the UK the *BNFC* suggests a dose of 7.5 mg/kg twice daily for those aged from 1 month to 12 years; older children may be given the adult dose (see above).

For prophylaxis of disseminated infection due to *Mycobacterium avium* complex, clarithromycin may be given in an oral dose of 7.5 mg/kg twice daily; when used for treatment, it should be given with other antimycobacterials and the dose may be increased to 15 mg/kg (to a maximum of 500 mg) twice daily.

For the eradication of *Helicobacter pylori* associated with peptic ulcer disease, the *BNFC* suggests that 7.5 mg/kg twice daily may also be given orally with another antibacterial and a proton pump inhibitor for 7 days to children aged 1 year and over.

Administration in renal impairment. Licensed product information states that in patients with severe renal impairment (creatinine clearance of less than 30 mL/minute) dosage of clarithromycin may need to be halved or the dosing interval doubled.

Ischaemic heart disease. For mention of studies investigating clarithromycin in the prevention of ischaemic heart disease, see under Azithromycin, p.208.

Multiple myeloma. Clarithromycin 500 mg orally twice daily has been added[1] to a regimen of lenalidomide and dexamethasone in treatment-naive patients with multiple myeloma (p.658). The regimen (BiRD) was considered effective and well tolerated, with a higher response rate at lower dexamethasone doses than had been previously reported with lenalidomide and dexamethasone alone. A regimen of clarithromycin, low-dose thalidomide, and dexamethasone (BLT-D) has also been evaluated.[2]

1. Niesvizky R, *et al.* BiRD (Biaxin [clarithromycin]/Revlimid [lenalidomide]/dexamethasone) combination therapy results in high complete- and overall-response rates in treatment-naive symptomatic multiple myeloma. *Blood* 2008; **111:** 1101–9.
2. Coleman M, *et al.* BLT-D (clarithromycin [Biaxin], low-dose thalidomide, and dexamethasone) for the treatment of myeloma and Waldenström's macroglobulinemia. *Leuk Lymphoma* 2002; **43:** 1777–82.

Respiratory disorders. For reference to the use of clarithromycin in the management of respiratory disorders, see under Erythromycin, p.273.

Preparations

USP 31: Clarithromycin Extended-Release Tablets; Clarithromycin for Oral Suspension; Clarithromycin Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Aeroxina; Centromicina†; Claribiotic; Claricina; Clarimax; Clarimid; Clarovil; Clatromicin†; Corixa; Finasept; Ira; Iset; Kailasa; Klaricid; Klonacid; Macromicina; Orabiot UD†; ***Austral.:*** Clarac; Clarithro; Kalixocin; Klacid; ***Austria:*** Clararcana; Klacid; Maclar; Monocid; ***Belg.:*** Biclar; Heliclar; Maclar; Monaxin†; ***Braz.:*** Clamicin; Claricina†; Clarineo; Claritromax; Claritron†; Clatorin†; Klaricid; Klaritril†; ***Canad.:*** Biaxin; ***Chile:*** Clarimax; Clarosip; Clatic; Euromicina; Infex; Klaricid; Mus†; Pre-Clar; ***Cz.:*** Clarexid; Clarosip; Fromilid; Klabax; Klacid; Lekoklar; Zeclar†; ***Denm.:*** Klacid; ***Fin.:*** Klacid; Zeclar; ***Fr.:*** Mononaxy; Monozeclar; Naxy; Zeclar; ***Ger.:*** Biaxin; Clarithrobeta; Cyllind; Klacid; Mavid; ***Gr.:*** Arecid; Chlamydicin; Claribactron; Clarimex; Claripen; Claromycin; Derizic; Egelif; Eliben; Ezumycin; Geromycin; Glartin; Klaretop; Klaricid; Klarifar; Klarifect; Klarithrin; Klaroxin; Klazidem; Larithro; Laromin; Lyoclar; Macladin; Maxilin; Odycin; Oklaricid†; Pharlemyron; Primocid; Riclemed; Rithroprol; Ritran; Zeclaren; ***Hong Kong:*** Binoclar; Clacin; Cleron; Klacid; Klerimed; Synclar; ***Hung.:*** Cidoclar; Fromilid; Klabax; Klacid; Klamiran†; Klari†; Klarigen; Lekoklar; ***India:*** Bioclar; Clarbact; Claribid; Claricip; Clarimac; Maclar; Synclar; ***Indon.:*** Abbotic; Bicrolid; Binoklar; Clacine; Clapharma; Comtro; Hecobac; ***Irl.:*** Clarosip; Clonocid; Clorom; Klacid; ***Israel:*** Karin; Klacid; Klaridex; ***Ital.:*** Klacid; Macladin; Veclam; ***Jpn:*** Clarith; ***Malaysia:*** Binocular; Crixan; Klacid; Klerimed; Maclar; ***Mex.:*** Adel; Arlecyn-K; Clatrocin; Crolisil; Doycur; Gervaken; Klabet; Klaricid; Klarix; Klarmyn; Klarpharma; Krobicin; Mabicrol; Neo-Clarosip; Quedox; Rolicytin; Torvic; Trimeba; Vikrol; Xuclamin; ***Neth.:*** Clarosip; Klacid; Klaricid; ***Norw.:*** Klacid; ***NZ:*** Clarac; Klacid; ***Philipp.:*** Bysclas; Claranta; Clariget; Klaricid; Klarmyn; Klaz; Larizin; Maxulid; Onexid; ***Pol.:*** Fromilid; Klabax; Klabion; Klacid; Klarmin; Lekoklar; Taclar; ***Port.:*** Ciclinil; Clacina; Clarbac; Clarobiotico; Clarosip; Klacid; Zeclar; ***Rus.:*** Clarbact (Кларбакт); Fromilid (Фромилид); Klabax (Клабакс); Klacid (Клацид); Klaromin (Кларомин); Klerimed (Клеримед); ***S.Afr.:*** Clacee; ClariHexal; Klacid; Klarithran; ***Singapore:*** Clari; Claripen; Cleron; Crixan; Klacid; Klerimed; ***Spain:*** Bremon; Claritur†; Klacid; Kofron; Talicix; ***Swed.:*** Klacid; ***Switz.:*** Claromycine; Klacid; Klaciped; ***Thai.:*** Clarith; Claron; Crixan; Fascar; Klacid; ***Turk.:*** Claricide; Klacid; Klarolid; Klaromin; Klax; Laricid; Macrol; Megacid; Uniklar; ***UAE:*** Clamycin; ***UK:*** Clarosip; Klaricid; ***USA:*** Biaxin; ***Venez.:*** Binoclar; Claranta; Claritic; Claritron; Clarivax; Klaricid.

Multi-ingredient: ***Arg.:*** Heliklar†; ***Austral.:*** Klacid HP 7; Losec Hp 7; Nexium Hp; Pylorid-KA; ***Austria:*** Helipac; ***Braz.:*** Anzopac†; Erradic; H-Bacter; Helicocid Triplice†; Helicopac; Heliklar; Omepramix; Pylorikit; Pyloripac; Pyloritrat; ***Canad.:*** Hp-Pac; Losec 1-2-3 A; Losec 1-2-3 M; ***Fin.:*** Helipak K; ***Ger.:*** ZacPac; ***India:*** OTC HP Kit; Pylokit; ***Malaysia:*** Klacid HP 7; Pylobact Combi; ***Mex.:*** Pylopac; Rezplen; ***Neth.:*** PantoPAC; ***NZ:*** Klacid HP 7†; Losec Hp 7; ***Philipp.:*** OAC Hp7; ***Rus.:*** Pylobact (Пилобакт); ***S.Afr.:*** Losec 20 Triple†; ***Swed.:*** Nexium Hp; ***Turk.:*** Helipak; ***UK:*** Helicleart†; HeliMet†; ***USA:*** Prevpac.

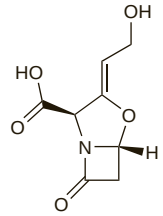
Clavulanic Acid *(BAN, rINN)*

Acide Clavulanique; Ácido clavulánico; Acidum Clavulanicum; BRL-14151; Klavulanik Asit; MM-14151. (*Z*)-(2*R*,5*R*)-3-(2-Hydroxyethylidene)-7-oxo-4-oxa-1-azabicyclo[3.2.0]heptane-2-carboxylic acid.

Клавулановая Кислота

$C_8H_9NO_5$ = 199.2.

CAS — 58001-44-8 (clavulanic acid); 57943-81-4 (sodium clavulanate).



Potassium Clavulanate *(BANM, rINNM)*

BRL-14151K; Clavulanate de Potassium; Clavulanate Potassium *(USAN)*; Clavulanato potásico; Kalii clavulanas; Kalio klavulanatas; Kaliumklavulanaatti; Kaliumklavulanat; Kálium-klavulanát; Kalium-klavulanát; Potassium, clavulanate de; Potasu klawulanian.

Калия Клавуланат

$C_8H_8KNO_5$ = 237.3.

CAS — 61177-45-5.

NOTE. Compounded preparations of potassium clavulanate may be represented by the following names:

- Co-amoxiclav *x*/*y* (*BAN*)—amoxicillin (as the trihydrate or the sodium salt) and potassium clavulanate; *x* and *y* are the strengths in milligrams of amoxicillin and clavulanic acid respectively
- Co-amoxiclav (*PEN*)—amoxicillin trihydrate and potassium clavulanate.

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

Eur. also includes Diluted Potassium Clavulanate.

Ph. Eur. 6.2 (Potassium Clavulanate). The potassium salt of a substance produced by the growth of certain strains of *Streptomyces clavuligerus* or by any other means. A white or almost white, hygroscopic, crystalline powder. Freely soluble in water; slightly soluble in alcohol; very slightly soluble in acetone. A 1% solution in water has a pH of 5.5 to 8.0. Store in airtight containers at a temperature of 2° to 8°.

Ph. Eur. 6.2 (Potassium Clavulanate, Diluted; Kalii Clavulanas Dilutus). A dry mixture of potassium clavulanate and microcrystalline cellulose or anhydrous or hydrated colloidal silicon dioxide. A white or almost white, hygroscopic, powder. A suspension corresponding to 1% of potassium clavulanate in water has a pH of 4.8 to 8.0. Store in airtight containers.

USP 31 (Clavulanate Potassium). A white to off-white powder. Freely soluble in water; soluble in methyl alcohol with decomposition. Stability in aqueous solutions is not good, optimum stability at a pH of 6.0 to 6.3. pH of a 1% solution in water is between 5.5 and 8.0. Store in airtight containers.

Profile

Clavulanic acid is produced by cultures of *Streptomyces clavuligerus*. It has a beta-lactam structure resembling that of the penicillin nucleus, except that the fused thiazolidine ring of the penicillins is replaced by an oxazolidine ring. In general, clavulanic acid has only weak antibacterial activity. It is a potent progressive inhibitor of plasmid-mediated and some chromosomal beta-lactamases produced by Gram-negative bacteria including *Haemophilus ducreyi*, *H. influenzae*, *Neisseria gonorrhoeae*, *Moraxella catarrhalis* (*Branhamella catarrhalis*), *Bacteroides fragilis*, and some Enterobacteriaceae. It is also an inhibitor of the beta-lactamases produced by *Staphylococcus aureus*. Clavulanic acid can permeate bacterial cell walls and can therefore inactivate both extracellular enzymes and those that are bound to the cell. Its mode of action depends on the particular enzyme inhibited, but it generally acts as a competitive, and often irreversible, inhibitor. Clavulanic acid consequently enhances the activity of penicillin and cephalosporin antibacterials against many resistant strains of bacteria. However, it is generally less effective against chromosomally mediated type 1 beta-lactamases; therefore, many *Citrobacter*, *Enterobacter*, *Morganella*, and *Serratia* spp., and *Pseudomonas aeruginosa* remain resistant. Some plasmid-mediated extended-spectrum beta-lactamases in *Klebsiella pneumoniae*, some other Enterobacteriaceae, and *Ps. aeruginosa* are also not inhibited by beta-lactamase inhibitors.

Clavulanic acid is given as potassium clavulanate orally and by injection with amoxicillin (co-amoxiclav) (p.202), and by injection with ticarcillin (p.352).

Use of clavulanate with penicillins has been associated with the development of cholestatic jaundice and hepatitis (see under Adverse Effects of Amoxicillin, p.202) and therefore the use of co-amoxiclav has declined (see below).

◊ Because of the risk of cholestatic jaundice co-amoxiclav is not a treatment of choice for common bacterial infections. The UK CSM[1] recommended that it should be reserved for bacterial infections likely to be caused by amoxicillin-resistant beta-lactamase-producing strains and that treatment should not usually exceed 14 days. It may be considered for the following main indications:

- sinusitis, otitis media, recurrent tonsillitis
- acute exacerbations of chronic bronchitis
- bronchopneumonia
- urinary-tract infections, especially when recurrent or complicated, but not prostatitis
- septic abortion, pelvic or puerperal sepsis, and intra-abdominal sepsis
- cellulitis, animal bites, and severe dental abscess with spreading cellulitis.

1. Committee on Safety of Medicines/Medicines Control Agency. Revised indications for co-amoxiclav (Augmentin). *Current Problems* 1997; **23:** 8. Also available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2023230&RevisionSelectionMethod=LatestReleased (accessed 11/07/06)

Preparations

BP 2008: Co-amoxiclav Injection; Co-amoxiclav Tablets;
USP 31: Amoxicillin and Clavulanate Potassium for Oral Suspension; Amoxicillin and Clavulanate Potassium Tablets; Ticarcillin and Clavulanic Acid for Injection; Ticarcillin and Clavulanic Acid Injection.

Proprietary Preparations (details are given in Part 3)
Arg.: Optamox; ***Indon.:*** Aclam; ***Turk.:*** Amoksilav.

Multi-ingredient: ***Arg.:*** Aclav; Amixen Clavulanico; Amoclav; Amoxi Plus; Amoxigrand Compuesto; Amoxitenk Plus; Bi Moxal; Bi Moxal Duo; Bioclavid; Bioxilina Plus; Clavulox; Clavulox Duo; Cloximar Duo; Darzitil Plus; Dibional; Fullcilina Plus†; Grinsil Clavulanico; Klonalmox; ***Austral.:*** Augmentin; Ausclav†; Clamohexal; Clamoxyl; Clavulin; Curam; Timentin; ***Austria:*** Amoclan; Amoxicillin comp; AmoxiClavulan; Amoxicomp; Amoxiplus; Amoxistad plus; Augmentin; Benclav; Benomox; Betamoclav; Clavamox; Clavex; Clavolek; Clavoplus; Clavulanex; CombAmox; Curam; Lanoclav; Lekamoxiclav; Oxyclav; Xiclav; ***Belg.:*** Amoclane; Augmentin; Clavucid; Co-Amoxi; Co-Amoxilan†; Docamoclaf; Timentin; ***Braz.:*** Augmentin; Betaclav; Clav-Air†; Clavoxil†; Clavulin; Novamox; Policlavumoxil; Sigma Clav; Timentin; ***Canad.:*** Apo-Amoxi Clav; Clavulin; Novo-Clavamoxin; ratio-Aclavulanate; Timentin; ***Chile:*** Ambilan; Ambilan Bid; Amolex; Augmentin; Augmentin Bid; Clavinex; Clavinex Duo; Clavoxilina Bid; ***Cz.:*** Amoksiklav; Augmentin; Augmentin-Duo; Betaklav; Curam; Enhancin; Forcid; Klamoxin†; Megamox; Timentin; ***Denm.:*** Bioclavid; Spektramox; ***Fin.:*** Amoxin Comp; Augmentin; Bioclavid; Clapharin Comp; Clavurion; Clavuxal; Forcid; Spektramox†; ***Fr.:*** Augmentin; Ciblor; Claventin; ***Ger.:*** Abiclav; Amoclav; Amoxclav; Amoxi-Clavulan; Amoxi-saar plus; Amoxicillin comp; Amoxiclav; Amoxidura Plus; Amoxillat-Clav†; Amuclan†; Augmentan; ***Gr.:*** Augmentin; Bioclavid; Forcid; Frolicin; Fugentin; Moxiclav; Tenervan; Timentin; ***Hong Kong:*** Amoksiklav; Augmentin; Clamovid; Curam; Fleming; Moxiclav; Qualimentin; Timentin; ***Hung.:*** Aktil; Amoclan†; Amoclav; Augmentin; Augmentin-Duo; Augmentin-Extra; Clavumox†; Co-Amoxi; Curam; Enhancin; Forcid; ***India:*** Augmentin; Boostim; Novaclav; Nuclav; Rapiclav†; Timentin; ***Indon.:*** Amocomb; Ancla; Augmentin; Auspilic; Bellamox; Betaclav; Biditin; Capsinat; Clabat; Claneksi; Clavamox; Comsikla; Danoclav; Daxet; Dexyclav; Improvox; Lansiclav; Nufaclav; Nuvoclav; Prafamoc; Protamox; Surpas; Syneclav; Viaclav; Vulamox; Zumafen; ***Irl.:*** Augmentin; Clavamel; Germentin; Pinaclav; Timentin†; ***Israel:*** Amoxiclav; Augmentin; Clavamox; Timentin; ***Ital.:*** Abba; Anival; Augmentin; Clavucar†; Clavulin; Neoduplamox; Timentin; Xinamod; ***Malaysia:*** Augmentin; Cavumox; Clamovid; Curam; Enhancin; Moxiclav; Vestaclav†; ***Mex.:*** Acarbixin; Acimox AC; Alvi-Tec; Amobay CL; Amoxiclav; Amoxiclide; Apoclavox; Augmentin; Avuxilan; Clambusil; Clamoxin; Clavant; Clavucyd; Clavulin; Clavuser; Enhancin; Gramaxin; Maxint†; Moxlin CLV; Riclasip; Servamox CLV; Sinufin; Timentin; Valclan; ***Neth.:*** Amoclan; Amuclan; Augmentin; Bioclavid; Forcid; Timentin; ***Norw.:*** Bremide†; ***NZ:*** Alpha-Amoxyclav; Augmentin; Synermox; Timentin; ***Philipp.:*** Amoclav; Augmentin; Augmex; Augurcin; Bactiv; Bactoclav; Bioclavid; Clamovid; Claneksi; Claventin; Clavoxel; Clovimax; Enhancin; Exten; Klavic; Natravox; Proxiclav; Sullivan; Suplentin; Timentin; Valmocel; Xilanic; ***Pol.:*** Amoksiklav; Augmentin; Curam; Forcid; Ramoclav; Taromentin; Timentin; ***Port.:*** Amoclavam; Amplamox Plus; Augmentin; Betamox; Clavamox; Clavepen; Forcid; Noprilam; Penilan; ***Rus.:*** Amoclan (Амоклан); Amoksiklav (Амоксиклав); Augmentin (Аугментин); Flemoclav (Флемоклав); Medoclav (Медоклав); Panklav (Панклав); Rapiclav (Рапиклав); Timentin (Тиментин); ***S.Afr.:*** Adco-Amoclav; Augmaxcil; Augmentin; Bio-Amoksiclav; Clamentin; Clavumox; Co-Amoxyclav; Curam; Forcid; Moxyclav†; Ranclav; Rolab-Amoclav; ***Singapore:*** Amocla; Augmentin; Augmex†; Clamonex; Clamovid; Curam; Enhancin; Fugentin; Moxiclav; ***Spain:*** Amoclave; Amoxyplus; Ardineclav; Augmentine; Bigpen†; Burmicin; Clavepen; Clavucid; Clavumox; Duonasa; Eupeclanic†; Inmupen†; Kelsopen; ***Swed.:*** Bioclavid; Spektramox; ***Switz.:*** Amicosol; Augmentin; Aziclav; Clavamox; clavu-basan†; Co-Amoxi; Co-Amoxicilline; Timenten†; ***Thai.:*** Amocla; Amoksiklav; Augclav; Augmentin; Augpen; Cavumox; Curam; Klamoks; Moxiclav; Moxicle; Pencla; Ranclav; ***Turk.:*** Amoklavin; Augmentin; Bioment; Croxilex; Klamoks; Klavunat; Klavupen; ***UAE:*** Julmentin; ***UK:*** Amiclav†; Augmentin; Augmentin-Duo; Timentin; ***USA:*** Amoclan; Augmentin; Timentin; ***Venez.:*** Augmentin; Augmentin Bid†; Clavumox; Curam; Fulgram.