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.

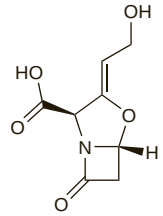
Clavulanic Acid *(BAN, rINN)*

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.

Clemizole Penicillin *(BAN, rINN)*

Clemizol penicilina; Clemizole Benzylpenicillin; Clémizole Pénicilline; Clemizolum Penicillinum; Klemitsolipenisilliini; Klemizolpenicillin; Penicillin G Clemizole. 1-[1-(4-Chlorobenzyl)benzimidazol-2-ylmethyl]pyrrolidinium (6*R*)-6-(2-phenylacetamido)penicillanate.

Клемизол Пенициллин

$C_{16}H_{18}N_2O_4S,C_{19}H_{20}ClN_3$ = 660.2.

CAS — 6011-39-8.

Profile

Clemizole penicillin is a long-acting preparation of benzylpenicillin (p.213) with similar properties and uses.

Preparations

Proprietary Preparations (details are given in Part 3)
Chile: Prevepen; ***Mex.:*** Megapenil; ***Switz.:*** Megacilline†.

Multi-ingredient: ***Chile:*** Prevepen Forte; ***Mex.:*** Anapenil; Megapenil Forte; ***Port.:*** Prevecilina; ***Spain:*** Neopenyl.

Clindamycin *(BAN, USAN, rINN)*

Clindamicina; Clindamycine; Clindamycinum; Klindamisin; Klindamycin; Klindamysiini; U-21251. Methyl 6-amino-7-chloro-6,7,8-trideoxy-*N*-[(2*S*,4*R*)-1-methyl-4-propylprolyl]-1-thio-L-*threo*-D-*galacto*-octopyranoside.

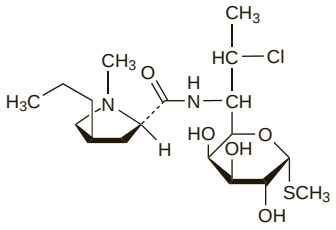
Клиндамицин

$C_{18}H_{33}ClN_2O_5S$ = 425.0.

CAS — 18323-44-9.

ATC — D10AF01; G01AA10; J01FF01.

ATC Vet — QD10AF01; QG01AA10; QJ01FF01.



NOTE. The name Clinimycin, which was formerly used for clindamycin, has also been used for a preparation of oxytetracycline.

Clindamycin Hydrochloride *(BANM, rINNM)*

Chlorodeoxylincomycin Hydrochloride; (7*S*)-Chloro-7-deoxylincomycin Hydrochloride; Clindamycine, chlorhydrate de; Clindamycini hydrochloridum; Hidrocloruro de clindamicina; Klindamicin-hidroklorid; Klindamicino hidrochloridas; Klindamisin Hidroklorür; Klindamycin-hydrochlorid; Klindamycinhydroklorid; Klindamycyny chlorowodorek; Klindamysiinihydrokloridi.

Клиндамицина Гидрохлорид

$C_{18}H_{33}ClN_2O_5S,HCl$ = 461.4.

CAS — 21462-39-5 (anhydrous clindamycin hydrochloride); 58207-19-5 (clindamycin hydrochloride monohydrate).

ATC — D10AF01; G01AA10; J01FF01.

ATC Vet — QD10AF01; QG01AA10; QJ01FF01.

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

Ph. Eur. 6.2 (Clindamycin Hydrochloride). A white or almost white, crystalline powder. It contains a variable quantity of water. Very soluble in water; slightly soluble in alcohol. A 10% solution in water has a pH of 3.0 to 5.0. Store in airtight containers.

USP 31 (Clindamycin Hydrochloride). A white or practically white crystalline powder, odourless or has a faint mercaptan-like odour. Freely soluble in water, in dimethylformamide, and in methyl alcohol; soluble in alcohol; practically insoluble in acetone. pH of a 10% solution in water is between 3.0 and 5.5. Store in airtight containers.

Clindamycin Palmitate Hydrochloride

(BANM, USAN, rINNM)

Clindamycine, Chlorhydrate de Palmitate de; Clindamycini Palmitatis Hydrochloridum; Hidrocloruro del palmitato de clindamicina; U-25179E. Clindamycin 2-palmitate hydrochloride.

Клиндамицина Палмитата Гидрохлорид

$C_{34}H_{63}ClN_2O_6S,HCl$ = 699.9.

CAS — 36688-78-5 (clindamycin palmitate); 25507-04-4 (clindamycin palmitate hydrochloride).

ATC — D10AF01; G01AA10; J01FF01.

ATC Vet — QD10AF01; QG01AA10; QJ01FF01.

Pharmacopoeias. In *US*.

USP 31 (Clindamycin Palmitate Hydrochloride). A white to off-white amorphous powder having a characteristic odour. Freely soluble in water, in chloroform, in ether, and in benzene; soluble 1 in 3 of alcohol and 1 in 9 of ethyl acetate; very soluble in dimethylformamide. pH of a 1% solution in water is between 2.8 and 3.8. Store in airtight containers.

Clindamycin Phosphate *(BANM, USAN, rINNM)*

Clindamycine, phosphate de; Clindamycini Dihydrogenophosphas; Clindamycini phosphas; Fosfato de clindamicina; Klindamicin-foszfát; Klindamicino fosfatas; Klindamisin Fosfat; Klindamycin dihydrogen fosfát; Klindamycinfosfat; Klindamysiinifosfaatti; U-28508. Clindamycin 2-(dihydrogen phosphate).

Клиндамицина Фосфат

$C_{18}H_{34}ClN_2O_8PS$ = 505.0.

CAS — 24729-96-2.

ATC — D10AF01; G01AA10; J01FF01.

ATC Vet — QD10AF01; QG01AA10; QJ01FF01.

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

Ph. Eur. 6.2 (Clindamycin Phosphate). A white or almost white, slightly hygroscopic powder. It exhibits polymorphism. Freely soluble in water; very slightly soluble in alcohol; practically insoluble in dichloromethane. A 1% solution in water has a pH of 3.5 to 4.5. Store at a temperature not exceeding 30° in airtight containers.

USP 31 (Clindamycin Phosphate). A white to off-white, odourless or practically odourless, hygroscopic, crystalline powder. Soluble 1 in 2.5 of water; slightly soluble in dehydrated alcohol; very slightly soluble in acetone; practically insoluble in chloroform, in ether, and in benzene. pH of a 1% solution in water is between 3.5 and 4.5. Store in airtight containers.

Incompatibility. Solutions of clindamycin salts have an acid pH and incompatibility may reasonably be expected with alkaline preparations, or with drugs unstable at low pH. Licensed product information for the injectable solution of clindamycin states that incompatibility has been reported between clindamycin and the following drugs: ampicillin, aminophylline, barbiturates, calcium gluconate, ceftriaxone, ciprofloxacin, idarubicin, magnesium sulfate, phenytoin, and ranitidine.

Clindamycin phosphate is incompatible with natural rubber closures.

Adverse Effects and Treatment

Clindamycin is reported to produce diarrhoea in up to 20% of patients after systemic use. In some patients severe antibiotic-associated or pseudomembranous colitis (p.171) may develop during therapy or up to several weeks after it, and has proved fatal. It has been reported to be more frequent in middle-aged and elderly women, particularly after surgery; it may also occur rarely after topical use. Clindamycin should be stopped immediately if significant diarrhoea or colitis occurs. Protein supplementation and use of an antibacterial active against *Clostridium* spp. should be considered for severe antibiotic-associated colitis.

Other gastrointestinal effects include nausea, vomiting, abdominal pain or cramps, and oesophagitis; an unpleasant or metallic taste has occasionally been reported after high intravenous doses.

Skin rashes and urticaria, the most common hypersensitivity reactions, occur in up to 10% of patients usually after 1 to 2 weeks of therapy. Erythema multiforme, Stevens-Johnson syndrome, and exfoliative and vesiculobullous dermatitis have been reported rarely, and a few cases of anaphylaxis have occurred.

Other adverse effects include transient leucopenia or occasionally agranulocytosis, eosinophilia, thrombocytopenia, polyarthritis, and abnormalities of liver function tests; in some cases overt jaundice and hepatic damage have been reported. Renal dysfunction, shown by azotaemia, oliguria, and/or proteinuria has been reported rarely.

Although local irritation is rare, intramuscular injection has led to induration and sterile abscess, and thrombophlebitis may occur after intravenous use. Too rapid intravenous infusion can result in rare instances of cardiopulmonary arrest and hypotension. Some parenteral formulations contain benzyl alcohol which may cause fatal 'gasping syndrome' in neonates (see p.1632).

Topical application may be associated with local irritation and contact dermatitis; sufficient clindamycin may be absorbed to produce systemic effects. Cervicitis, vaginitis, or vulvovaginal irritation has been reported with intravaginal use; a small amount of systemic absorption also occurs.

Effects on the cardiovascular system. Cardiac arrest occurred in a 50-year-old woman after rapid injection of 600 mg of undiluted clindamycin phosphate into a central intravenous line. Further injections were given over 30 minutes without cardiovascular complications.[1] There has also been a case of severely prolonged QT interval attributed to the addition of clindamycin to therapy in an elderly woman;[2] the patient developed AV block and subsequent torsade de pointes, and required resuscitation. When clindamycin was stopped, signs of heart block resolved, and the QT interval returned to normal over several days.

1. Aucoin P, *et al.* Clindamycin-induced cardiac arrest. *South Med J* 1982; **75:** 768.
2. Gabel A, *et al.* Ventricular fibrillation due to long QT syndrome probably caused by clindamycin. *Am J Cardiol* 1999; **83:** 813–15.

Effects on the ears. A 14-year-old boy who was treated with topical clindamycin for acne vulgaris developed unilateral tinnitus during therapy and unilateral sensorineural hearing loss 2 months later;[1] symptoms subsequently recurred upon 2 rechallenges.

1. Scissors B, Shwayder T. Topical clindamycin reproducibly causing tinnitus in a 14-year-old boy. *J Am Acad Dermatol* 2006; **54** (suppl): S243–S244.

Effects on the lymphatic system. A report of lymphadenitis associated with clindamycin.[1]

1. Southern PM. Lymphadenitis associated with the administration of clindamycin. *Am J Med* 1997; **103:** 164–5.

Effects on the skin. There have been reports of toxic epidermal necrolysis[1] and acute generalised exanthematous pustulosis[2,3] associated with clindamycin.

1. Paquet P, *et al.* Toxic epidermal necrolysis following clindamycin treatment. *Br J Dermatol* 1995; **132:** 665–6.
2. Valois M, *et al.* Clindamycin-associated acute generalized exanthematous pustulosis. *Contact Dermatitis* 2003; **48:** 169.
3. Kapoor R, *et al.* Acute generalized exanthematous pustulosis induced by clindamycin. *Arch Dermatol* 2006; **142:** 1080–81.

Precautions

Clindamycin should not be given to patients hypersensitive to it or to the closely related drug lincomycin. It should be used with caution in patients with a history of gastrointestinal disease, particularly colitis, and stopped immediately if significant diarrhoea or colitis occurs. Middle-aged and elderly female patients may be at greater risk of severe diarrhoea or pseudomembranous colitis. Caution has also been advised in atopic patients. Periodic tests of liver and kidney function and blood counts have been recommended in patients receiving prolonged therapy, and in infants. Caution is required during parenteral use in neonates, since some parenteral formulations contain benzyl alcohol which may cause fatal 'gasping syndrome' (see p.1632).

AIDS. Clindamycin was poorly tolerated by patients with AIDS in a study of its use for *prophylaxis* of toxoplasmic encephalitis.[1] Despite the use of relatively low doses of clindamycin (300 mg twice daily), 23 of 52 patients reported adverse effects that necessitated temporary or permanent withdrawal of the drug, the most frequent adverse reactions being diarrhoea and skin rash. The clindamycin arm of the study had to be terminated prematurely. Nevertheless, clindamycin has been used successfully in patients with AIDS for the *treatment* of both toxoplasmic encephalitis (see Toxoplasmosis, below) and pneumocystis pneumonia (below).

1. Jacobson MA, *et al.* Toxicity of clindamycin as prophylaxis for AIDS-associated toxoplasmic encephalitis. *Lancet* 1992; **339:** 333–4.

Breast feeding. US licensed product information states that concentrations of clindamycin in breast milk were 0.7 to 3.8 micrograms/mL after doses of 150 mg orally to 600 mg intravenously. No adverse effects have been seen in breast-fed infants whose mothers were receiving clindamycin, and the American Academy of Pediatrics[1] considers that it is therefore usually compatible with breast feeding. Nevertheless, UK product information states that although it is unlikely that a breast-fed infant could absorb significant amounts, caution should be exercised when clindamycin is given during breast feeding.

1. American Academy of Pediatrics. The transfer of drugs and other chemicals into human milk. *Pediatrics* 2001; **108:** 776–89. Correction. *ibid.*; 1029. Also available at: http://aappolicy.aappublications.org/cgi/content/full/pediatrics%3b108/3/776 (accessed 25/05/04)

Interactions

Clindamycin has neuromuscular blocking activity in high doses and may enhance the effect of other drugs with this action (see Atracurium, p.1903), leading to a potential danger of respiratory depression. Clindamycin may antagonise the effects of parasympathomimetics. For mention of synergistic and antagonistic antimicrobial activity with other antibacterials, see Antimicrobial Action, below.