B; ***Canad.:*** Fucidin H; ***Chile:*** Fucicort; Fucidin H; ***Cz.:*** Fucicort; Fucidin H; ***Denm.:*** Fucicort; Fucidin-Hydrocortison; ***Fin.:*** Fucicort; Fucidin-Hydrocortison; ***Ger.:*** Fucicort; Fucidine plus†; ***Gr.:*** Alpider; Befucil; Betacort; Betafusin; Betasid; Betfu; Fubecot; Fucicort; Fucicream; Fucidin H; Fusibet; Hydrofusin; Roseti; Sensibio; Staficort; ***Hong Kong:*** Fucicort; Fucidin H; ***Hung.:*** Fucicort; Fucidin H; ***Indon.:*** Fucicort; ***Irl.:*** Fucibet; Fucidin H; ***Israel:*** Fucicort; Fucidin H†; ***Ital.:*** Fucicort; Fucidin H; Piodermina; ***Malaysia:*** Axcel Fusi-Corte; Foban-Hydro; Fobancort; Fucicort; Fucidin H; Fusidic B; ***Mex.:*** Fucicort; ***Norw.:*** Fucidin-Hydrocortison; ***NZ:*** Fucicort; ***Philipp.:*** Fucicort; Fucidin H; Hoebedic; ***Port.:*** Fucicort; Fucidine H; ***Rus.:*** Fucicort (Фуцикорт); Fucidin H (Фуцидин Г); ***S.Afr.:*** Fucidin H; ***Singapore:*** Fobancort; Fucicort; Fucidin H; ***Spain:*** Fucibet; Fucidine H; ***Swed.:*** Fucidin-Hydrocortison; ***Switz.:*** Fucicort; Fucidin H; ***Thai.:*** Fucicort; Fucidin H; ***UAE:*** Futasone; ***UK:*** Fucibet; Fucidin H.

Garenoxacin Mesilate *(BANM, rINNM)*

BMS-284756-01; Garenoxacin Mesylate *(USAN)*; Garénoxacine, Mésilate de; Garenoxacini Mesilas; Mesilato de garenoxacino; T-3811ME. 1-Cyclopropyl-8-(difluoromethoxy)-7-[(1*R*)-1-methyl-2,3-dihydro-1*H*-isoindol-5-yl]-4-oxo-1,4-dihydroquinoline-3-carboxylic acid methanesulfonate monohydrate.

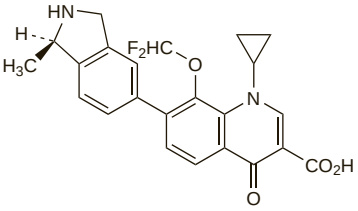
Гареноксацина Мезилат

$C_{23}H_{20}F_2N_2O_4,CH_4O_3S,H_2O$ = 540.5.

CAS — 194804-75-6 (garenoxacin); 223652-82-2 (garenoxacin mesilate); 223652-90-2 (garenoxacin mesilate monohydrate).

ATC — J01MA19.

ATC Vet — QJ01MA19.



(garenoxacin)

Profile

Garenoxacin is a fluoroquinolone antibacterial with properties similar to those of ciprofloxacin (p.247). Garenoxacin is used as the mesilate but doses are given in terms of the base: about 507 mg of the mesilate is equivalent to 400 mg of garenoxacin. It is given orally in the treatment of susceptible infections in usual doses equivalent to 400 mg of garenoxacin daily.

Gatifloxacin *(USAN, rINN)*

AM-1155; BMS-206584-01; CG-5501; Gatifloxacine; Gatifloxacino; Gatifloxacinum. (±)-1-Cyclopropyl-6-fluoro-1,4-dihydro-8-methoxy-7-(3-methyl-1-piperazinyl)-4-oxo-3-quinolinecarboxylic acid sesquihydrate.

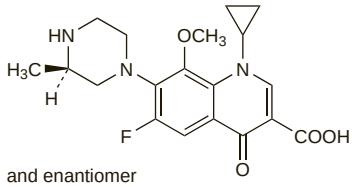
Гатифлоксацин

$C_{19}H_{22}FN_3O_4,1/_2H_2O$ = 402.4.

CAS — 160738-57-8 (anhydrous gatifloxacin); 180200-66-2 (gatifloxacin sesquihydrate).

ATC — J01MA16; S01AX21.

ATC Vet — QJ01MA16; QS01AX21.



and enantiomer

Adverse Effects and Precautions

As for Ciprofloxacin, p.244.

Symptomatic hyperglycaemia and/or hypoglycaemia have been reported in patients (usually diabetics) taking gatifloxacin. However, hypoglycaemia, and particularly hyperglycaemia, have occurred in non-diabetic patients. Severe life-threatening events, including hyperosmolar nonketotic hyperglycaemic coma, diabetic ketoacidosis, hypoglycaemic coma, convulsions, and mental status changes have been reported very rarely. Although in most cases the blood-glucose disturbance was reversible, fatalities have been reported. Gatifloxacin should not be given to diabetic patients. Other risk factors for developing blood-glucose disturbances include older age (patients 65 years of age or over), renal impairment, or use of other drugs that alter blood-glucose concentrations, particularly hypoglycaemics. Patients with risk factors should have their blood-glucose concentrations closely monitored and if signs or symptoms of glucose disturbances develop, gatifloxacin should be stopped.

Effects on glucose metabolism. Hypoglycaemia and hyperglycaemia have been associated with gatifloxacin in both diabetic and non-diabetic patients.[1-6] A review[7] of spontaneous adverse effects reported to the FDA in the USA between November 1997 and September 2003 found the rate of blood-glucose disturbances with gatifloxacin to be 10-fold higher when compared with ciprofloxacin, levofloxacin, and moxifloxacin. Subsequent population-based case-control studies[8] in elderly patients given fluoroquinolones (ciprofloxacin, gatifloxacin, levofloxacin, or moxifloxacin), second-generation cephalosporins, or macrolides also found an increased risk of blood-glucose disturbances with gatifloxacin.

While blood-glucose disturbances appear to be mainly associated with gatifloxacin, the possibility that they may also be a class effect of fluoroquinolones cannot be excluded; patients most at risk are the elderly, those with diabetes and/or those taking hypoglycaemic drugs, and patients with impaired renal function.[9] Twenty two case reports of dysglycaemia associated with the use of levofloxacin were received by Health Canada between January 1997 and June 2006; reported cases included 15 diabetic patients.[10] In contrast a review of the effects of moxifloxacin on blood glucose, including data from large postmarketing studies, suggested it had no significant effect.[11]

1. Baker SE, Hangii MC. Possible gatifloxacin-induced hypoglycemia. *Ann Pharmacother* 2002; **36:** 1722–6.
2. Donaldson AR, *et al.* Possible gatifloxacin-induced hyperglycemia. *Ann Pharmacother* 2004; **38:** 602–5.
3. Happe MR, *et al.* Gatifloxacin-induced hyperglycemia. *Ann Intern Med* 2004; **141:** 968–9.
4. Khovidhunkit W, Sunthornyothin S. Hypoglycemia, hyperglycemia, and gatifloxacin. *Ann Intern Med* 2004; **141:** 969.
5. Greenberg AL, *et al.* Gatifloxacin therapy associated with hypoglycemia. *Clin Infect Dis* 2005; **40:** 1210–11.
6. Blommel AL, Lutes RA. Severe hyperglycemia during renally adjusted gatifloxacin therapy. *Ann Pharmacother* 2005; **39:** 1349–52.
7. Frothingham R. Glucose homeostasis abnormalities associated with use of gatifloxacin. *Clin Infect Dis* 2005; **41:** 1269–76.
8. Park-Wyllie LY, *et al.* Outpatient gatifloxacin therapy and dysglycemia in older adults. *N Engl J Med* 2006; **354:** 1352–61.
9. Lewis RJ, Mohr JF. Dysglycaemias and fluoroquinolones. *Drug Safety* 2008; **31:** 283–92.
10. Health Canada. Levofloxacin: dysglycemia and liver disorders. *Can Adverse React News* 2007; **17:** 1–2. Also available at: http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/medeff/ carn-bcei_v17n1-eng.pdf (accessed 17/06/08)
11. Gavin JR, *et al.* Moxifloxacin and glucose homeostasis: a pooled-analysis of the evidence from clinical and postmarketing studies. *Drug Safety* 2004; **27:** 671–86.

Interactions

As for Ciprofloxacin, p.246.

Use of gatifloxacin with drugs that alter blood-glucose concentrations increases the risk of blood-glucose disturbances.

Antidiabetics. Given the adverse effects of gatifloxacin, pharmacodynamic interactions with antidiabetics might reasonably be anticipated. Severe and persistent hypoglycaemia occurred in 3 patients taking oral hypoglycaemics (*repaglinide*, *glibenclamide* and *pioglitazone*, and *glimepiride*) when gatifloxacin was added to their therapy.[1]

1. Menzies DJ, *et al.* Severe and persistent hypoglycemia due to gatifloxacin interaction with oral hypoglycemic agents. *Am J Med* 2002; **113:** 232–4.

Antimicrobial Action

As for Ciprofloxacin, p.246.

Gatifloxacin is reported to have greater activity against Gram-positive bacteria, including pneumococci, than ciprofloxacin.

◊ References.

1. Stein GE, *et al.* Bactericidal activities of methoxyfluoroquinolones gatifloxacin and moxifloxacin against aerobic and anaerobic respiratory pathogens in serum. *Antimicrob Agents Chemother* 2003; **47:** 1308–12.

Pharmacokinetics

Gatifloxacin is readily absorbed from the gastrointestinal tract with an absolute bioavailability of 96%. Peak plasma concentrations occur within 1 to 2 hours of an oral dose. Gatifloxacin is widely distributed into body tissues and is about 20% bound to plasma proteins. It undergoes limited metabolism and has an elimination half-life of 7 to 14 hours. Gatifloxacin is excreted primarily unchanged in the urine with less than 1% as metabolites. About 5% is also excreted unchanged in the faeces. Distribution into milk occurs in *animals*.

Uses and Administration

Gatifloxacin is a fluoroquinolone antibacterial with actions and uses similar to those of ciprofloxacin (p.247).

It is given orally, or by intravenous infusion as a 2 mg/mL solution over 60 minutes, for the treatment of susceptible infections, including respiratory- and urinary-tract infections and skin infections. The usual adult dose is 400 mg once daily. A single dose of 400 mg or a dose of 200 mg daily for 3 days may be adequate for uncomplicated urinary-tract infections.

For details of reduced doses to be used in renal impairment, see below.

A single dose of 400 mg may also be given for the treatment of uncomplicated gonorrhoea.

Gatifloxacin is also used as 0.3% eye drops for the treatment of bacterial conjunctivitis.

◊ Reviews.

1. Keam SJ, *et al.* Gatifloxacin: a review of its use in the treatment of bacterial infections in the US. *Drugs* 2005; **65:** 695–724.

Administration in renal impairment. Doses of gatifloxacin should be reduced in patients with renal impairment; the usual initial dose of 400 mg should be followed by reduced maintenance doses of 200 mg daily in those with a creatinine clearance of less than 40 mL/minute and in those on haemodialysis or continuous peritoneal dialysis.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Gatif; Tequin†; Zymaran; ***Austral.:*** Tequin; ***Braz.:*** Tequin; Zymar; ***Canad.:*** Tequin; Zymar; ***Chile:*** Starox†; Zymar; ***Ger.:*** Bonoq†; ***India:*** Biogat†; Gaticin; Gatiquin; Gatt; Zyquin; ***Indon.:*** Gaticin; Gatimax; ***Jpn:*** Gatiflo; ***Malaysia:*** Tequin†; ***Mex.:*** Tequin; Zymar; ***NZ:*** Tequin; ***Philipp.:*** Tequin; Zymar; ***S.Afr.:*** Tequin; ***Singapore:*** Tequin†; Zymar; ***Thai.:*** Tequin†; Zymar; ***USA:*** Tequin†; Zymar.

Multi-ingredient: ***India:*** Gatiquin Oz Kit.

Gemifloxacin Mesilate *(rINNM)*

Gemifloxacin Mesylate *(USAN)*; Gémifloxacine, Mésilate de; Gemifloxacini Mesilas; LB-20304 (gemifloxacin); LB-20304a; Mesilato de gemifloxacino; SB-265805 (gemifloxacin); SB-265805S. (±)-7-[3-(Aminomethyl)-4-oxo-1-pyrrolidinyl]-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid 7[4]-(*Z*)-(*O*-methyloxime) methanesulfonate.

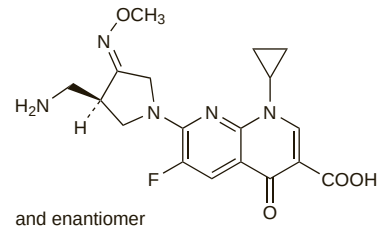
Гемифлоксацина Мезилат

$C_{18}H_{20}FN_5O_4,CH_4O_3S$ = 485.5.

CAS — 204519-64-2 (gemifloxacin); 204519-65-3 (gemifloxacin mesilate).

ATC — J01MA15.

ATC Vet — QJ01MA15.



and enantiomer

(gemifloxacin)

Adverse Effects and Precautions

As for Ciprofloxacin, p.244.

Skin rashes may be more common with gemifloxacin and treatment should be stopped if they occur.

Interactions

As for Ciprofloxacin, p.246.

Antimicrobial Action

As for Ciprofloxacin, p.246.

Gemifloxacin is reported to have greater activity against Gram-positive bacteria, including pneumococci, than ciprofloxacin.

◊ References.

1. Morrissey I, Tillotson G. Activity of gemifloxacin against Streptococcus pneumoniae and Haemophilus influenzae. *J Antimicrob Chemother* 2004; **53:** 144–8.

Pharmacokinetics

Gemifloxacin is rapidly absorbed from the gastrointestinal tract with an absolute bioavailability of about 71%. Peak plasma concentrations occur 0.5 to 2 hours after an oral dose. Gemifloxacin is widely distributed into body tissues including the bronchial

mucosa and lungs, and is about 55 to 73% bound to plasma proteins. It undergoes limited hepatic metabolism and has an elimination half-life of about 7 hours. It is excreted as unchanged drug and metabolites in the faeces and urine. Urinary excretion is by active tubular secretion and is reduced by probenecid. Distribution into milk has been found in *rats*.

Uses and Administration

Gemifloxacin is a fluoroquinolone antibacterial with actions and uses similar to those of ciprofloxacin (p.247).

It is given orally, as the mesilate, for the treatment of community-acquired pneumonia and acute bacterial exacerbations of chronic bronchitis. Doses are expressed in terms of the base; 399 mg of gemifloxacin mesilate is equivalent to about 320 mg of gemifloxacin. The usual dose is 320 mg once daily for 5 days in patients with bronchitis or for 7 days in those with pneumonia.

For details of reduced doses in patients with renal impairment, see below.

◊ Reviews.

1. Lowe MN, Lamb HM. Gemifloxacin. *Drugs* 2000; **59:** 1137–47.
2. Yoo BK, *et al*. Gemifloxacin: a new fluoroquinolone approved for treatment of respiratory infections. *Ann Pharmacother* 2004; **38:** 1226–35.
3. File TM, Tillotson GS. Gemifloxacin: a new, potent fluoroquinolone for the therapy of lower respiratory tract infections. *Expert Rev Anti Infect Ther* 2004; **2:** 831–43.
4. Bhavnani SM, Andes DR. Gemifloxacin for the treatment of respiratory tract infections: in vitro susceptibility, pharmacokinetics and pharmacodynamics, clinical efficacy, and safety. *Pharmacotherapy* 2005; **25:** 717–40.
5. Blondeau JM, Tillotson G. Role of gemifloxacin in the management of community-acquired lower respiratory tract infections. *Int J Antimicrob Agents* 2008; **31:** 299–306.
6. Lode HM, *et al*. Gemifloxacin for community-acquired pneumonia. *Expert Opin Invest Drugs* 2008; **17:** 779–86.
7. Tillotson GS. Role of gemifloxacin in community-acquired pneumonia. *Expert Rev Anti Infect Ther* 2008; **6:** 405–18.

Administration in renal impairment. Doses of gemifloxacin should be halved in patients with a creatinine clearance of 40 mL/minute or less, including those receiving haemodialysis or continuous peritoneal dialysis.

Preparations

Proprietary Preparations (details are given in Part 3)
Braz.: Factive; ***Rus.:*** Factiv (Фактив); ***S.Afr.:*** Factive; ***USA:*** Factive.

Gentamicin Sulfate *(USAN, pINNM)*

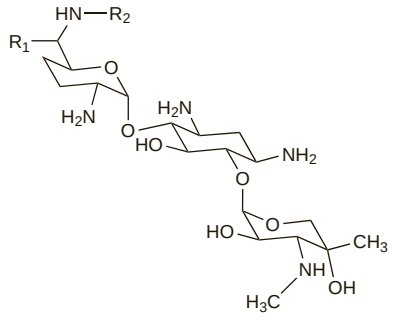
Gentamicin sulfát; Gentamicin Sulphate *(BANM)*; Gentamicine, sulfate de; Gentamicini sulfas; Gentamicino sulfatas; Gentamicin-sulfat; Gentamicin-szulfát; Gentamisiinisulfaatti; Gentamisin Sülfat; Gentamycyny siarczan; NSC-82261; Sch-9724; Sulfato de gentamicina.

Гентамицина Сульфат

CAS — 1403-66-3 (gentamicin); 1405-41-0 (gentamicin sulfate).

ATC — D06AX07; J01GB03; S01AA11; S02AA14; S03AA06.

ATC Vet — QD06AX07; QJ01GB03; QS01AA11; QS02AA14; QS03AA06.



Gentamicin C_1 $R_1 = R_2 = CH_3$
Gentamicin C_2 $R_1 = CH_3$, $R_2 = H$
Gentamicin C_{1a} $R_1 = R_2 = H$

(gentamicin)

NOTE. GNT is a code approved by the BP 2008 for use on single unit doses of eye drops containing gentamicin sulfate where the individual container may be too small to bear all the appropriate labelling information.

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

Ph. Eur. 6.2 (Gentamicin Sulphate). A mixture of the sulfates of antimicrobial substances produced by *Micromonospora purpurea*, the main components being gentamicins C1, C1a, C2, C2a, and C2b. It contains 20 to 40% of gentamicin C1, 10 to 30% of gentamicin C1a; the sum of gentamicins C2, C2a, and C2b is 40 to 60%. The potency is not less than 590 units/mg, calculated with reference to the anhydrous substance. A white or almost white hygroscopic powder. Freely soluble in water; practically insoluble in alcohol. A 4% solution in water has a pH of 3.5 to 5.5. Store in airtight containers.

USP 31 (Gentamicin Sulfate). The sulfate salt, or a mixture of such salts, of antibiotic substances produced by the growth of *Micromonospora purpurea*. The content of gentamicin C1 is between 25 and 50%, the content of gentamicin C1a is between 10 and 35%, and the sum of the contents of gentamicin C2a and gentamicin C2 is between 25 and 55%. It has a potency equivalent to not less than 590 micrograms of gentamicin per mg, calculated on the dried basis. A white to buff powder. Freely soluble in water; insoluble in alcohol, in acetone, in chloroform, in ether, and in benzene. pH of a 4% solution in water is between 3.5 and 5.5. Store in airtight containers.

Incompatibility. The aminoglycosides are inactivated *in vitro* by various penicillins and cephalosporins via an interaction with the beta-lactam ring, the extent of inactivation depending on temperature, concentration, and duration of contact. The different aminoglycosides vary in their stability, with amikacin apparently the most resistant and tobramycin the most susceptible to inactivation; gentamicin and netilmicin are of intermediate stability. The beta lactams also vary in their ability to produce inactivation, with ampicillin, benzylpenicillin, and antipseudomonal penicillins such as carbenicillin and ticarcillin producing marked inactivation. Inactivation has also been reported with clavulanic acid.

Gentamicin is also incompatible with furosemide, heparin, sodium bicarbonate (the acid pH of gentamicin solutions may liberate carbon dioxide), and some solutions for parenteral nutrition. Interactions with preparations having an alkaline pH (such as sulfadiazine sodium), or drugs unstable at acid pH (for example erythromycin salts), might reasonably be expected.

Given their potential for incompatibility, gentamicin and other aminoglycosides should not generally be mixed with other drugs in syringes or infusion solutions nor given through the same intravenous line. When aminoglycosides are given with a beta lactam, they should generally be given at separate sites.

General references.

1. Henderson JL, *et al*. In vitro inactivation of gentamicin, tobramycin, and netilmicin by carbenicillin, azlocillin, or mezlocillin. *Am J Hosp Pharm* 1981; **38:** 1167–70.
2. Tindula RJ, *et al*. Aminoglycoside inactivation by penicillins and cephalosporins and its impact on drug-level monitoring. *Drug Intell Clin Pharm* 1983; **17:** 906–8.
3. Navarro AS, *et al*. In-vitro interaction between dibekacin and penicillins. *J Antimicrob Chemother* 1986; **17:** 83–9.
4. Courcol RJ, Martin GR. Comparative aminoglycoside inactivation by potassium clavulanate. *J Antimicrob Chemother* 1986; **17:** 682–4.

Stability. There was an average 16% potency loss of gentamicin sulfate from solutions containing 10 and 40 mg/mL when stored at 4° or 25° in plastic disposable syringes for 30 days, and a brown precipitate formed in several. Storage in glass disposable syringes for 30 days produced an average 7% potency loss, which was considered acceptable, but storage for longer resulted in precipitate formation in some cases and was not recommended.[1]

1. Weiner B, *et al*. Stability of gentamicin sulfate injection following unit dose repackaging. *Am J Hosp Pharm* 1976; **33:** 1254–9.

Adverse Effects

The aminoglycosides can produce irreversible, cumulative ototoxicity. This affects both the cochlea (manifest as hearing loss, initially of higher tones, and which, because speech recognition relies greatly on lower frequencies, may not be at first apparent) and the vestibular system (manifest as dizziness or vertigo). The incidence and relative toxicity with different aminoglycosides is a matter of some dispute, but netilmicin is probably less cochleotoxic than gentamicin or tobramycin, and amikacin more so. Netilmicin also exhibits less vestibular toxicity than gentamicin, tobramycin, or amikacin, while streptomycin produces a high incidence of vestibular damage. Vestibular damage is more common than hearing loss in patients receiving gentamicin.

Reversible nephrotoxicity may occur and acute renal failure has been reported, often in association with the use of other nephrotoxic drugs. Renal impairment is usually mild, although acute tubular necrosis and interstitial nephritis have occurred. Decreased glomerular filtration rate is usually seen only after several days, and may even occur after therapy has stopped. Electrolyte disturbances (notably hypomagnesaemia, but also hypocalcaemia and hypokalaemia) have occurred. The nephrotoxicity of gentamicin is reported to be largely due to the gentamicin C_2 component.

Although particularly associated with high plasma concentrations, many risk factors have been suggested for ototoxicity and nephrotoxicity in patients receiving aminoglycosides—see Precautions below.

Aminoglycosides possess a neuromuscular-blocking action and respiratory depression and muscular paralysis have been reported, notably after absorption from serous surfaces. Neomycin has the most potent action and several deaths have been associated with its use.

Hypersensitivity reactions have occurred, especially after local use, and cross-sensitivity between aminoglycosides may occur. Very rarely, anaphylactic reactions to gentamicin have occurred. Some hypersensitivity reactions have been attributed to the presence of sulfites in parenteral formulations, and endotoxic shock has also been reported.

Infrequent effects reported for gentamicin include blood dyscrasias, purpura, nausea and vomiting, stomatitis, and signs of liver dysfunction such as increased serum-aminotransferase values and increased serum-bilirubin concentrations. Neurotoxicity has occurred, with both peripheral neuropathies and central symptoms being reported including encephalopathy, confusion, lethargy, hallucinations, convulsions, and mental depression.

Atrophy or fat necrosis has been reported at injection sites. There have been isolated reports of meningeal irritation, arachnoiditis, polyradiculitis, and ventriculitis after intrathecal, intracisternal, or intraventricular use of aminoglycosides. Subconjunctival injection of gentamicin may lead to pain, hyperaemia, and conjunctival oedema, while severe retinal ischaemia has followed intra-ocular injection.

Effects on the ears. Reviews and references to aminoglycoside-induced ototoxicity.

1. Cone LA. A survey of prospective, controlled clinical trials of gentamicin, tobramycin, amikacin, and netilmicin. *Clin Ther* 1982; **5:** 155–62.
2. Kahlmeter G, Dahlager JI. Aminoglycoside toxicity—a review of clinical studies published between 1975 and 1982. *J Antimicrob Chemother* 1984; **13** (suppl A): 9–22.
3. Brummett RE, Fox KE. Aminoglycoside-induced hearing loss in humans. *Antimicrob Agents Chemother* 1989; **33:** 797–800.
4. Mattie H, *et al*. Determinants of efficacy and toxicity of aminoglycosides. *J Antimicrob Chemother* 1989; **24:** 281–93.
5. Schacht J. Aminoglycoside ototoxicity: prevention in sight? *Otolaryngol Head Neck Surg* 1998; **118:** 674–7.
6. Nakashima T, *et al*. Vestibular and cochlear toxicity of aminoglycosides—a review. *Acta Otolaryngol* 2000; **120:** 904–11.
7. Darlington CL, Smith PF. Vestibulotoxicity following aminoglycoside antibiotics and its prevention. *Curr Opin Investig Drugs* 2003; **4:** 841–6.
8. Rizzi MD, Hirose K. Aminoglycoside ototoxicity. *Curr Opin Otolaryngol Head Neck Surg* 2007; **15:** 352–7.

Effects on the kidneys. Reviews and references to aminoglycoside-induced nephrotoxicity.

1. Cone LA. A survey of prospective, controlled clinical trials of gentamicin, tobramycin, amikacin, and netilmicin. *Clin Ther* 1982; **5:** 155–62.
2. Lietman PS, Smith CR. Aminoglycoside nephrotoxicity in humans. *Rev Infect Dis* 1983; **5** (suppl 2): S284–93.
3. Kahlmeter G, Dahlager JI. Aminoglycoside toxicity—a review of clinical studies published between 1975 and 1982. *J Antimicrob Chemother* 1984; **13** (suppl A): 9–22.
4. Kohlhepp SJ, *et al*. Nephrotoxicity of the constituents of the gentamicin complex. *J Infect Dis* 1984; **149:** 605–14.
5. Mattie H, *et al*. Determinants of efficacy and toxicity of aminoglycosides. *J Antimicrob Chemother* 1989; **24:** 281–93.
6. Appel GB. Aminoglycoside nephrotoxicity. *Am J Med* 1990; **88** (suppl 3C): 16S–20S.
7. Bertino JS, *et al*. Incidence of and significant risk factors for aminoglycoside-associated nephrotoxicity in patients dosed by using individualized pharmacokinetic monitoring. *J Infect Dis* 1993; **167:** 173–9.
8. Swan SK. Aminoglycoside nephrotoxicity. *Semin Nephrol* 1997; **17:** 27–33.
9. Baciewicz AM, *et al*. Aminoglycoside-associated nephrotoxicity in the elderly. *Ann Pharmacother* 2003; **37:** 182–6.
10. Rougier F, *et al*. Aminoglycoside nephrotoxicity. *Curr Drug Targets Infect Disord* 2004; **4:** 153–62.
11. Martínez-Salgado C, *et al*. Glomerular nephrotoxicity of aminoglycosides. *Toxicol Appl Pharmacol* 2007; **223:** 86–98.

Endotoxin reactions. Reports of endotoxin reactions associated with intravenous gentamicin have been received by the CDC and the FDA in the USA.[1] Although endotoxin concentrations in the injections used were within USP limits, giving a single daily dose rather than divided doses was thought to have resulted in toxic serum concentrations of endotoxins.[1,2]

1. CDC. Endotoxin-like reactions associated with intravenous gentamicin—California, 1998. *MMWR* 1998; **47:** 877–80.
2. Krieger JA, Duncan L. Gentamicin contaminated with endotoxin. *N Engl J Med* 1999; **340:** 1122.