Administration in hepatic impairment. Dosage of tigecycline should be adjusted in patients with severe hepatic impairment (Child-Pugh category C); the initial intravenous loading dose should be 100 mg with reduced maintenance doses of 25 mg every 12 hours.

Preparations

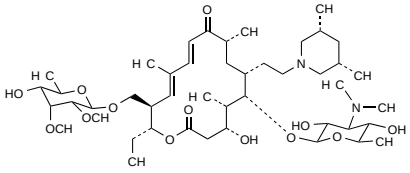
Proprietary Preparations (details are given in Part 3)
Arg.: Tygacil; ***Austral.:*** Tygacil; ***Braz.:*** Tygacil; ***Chile:*** Tygacil; ***Cz.:*** Tygacil; ***Gr.:*** Tygacil; ***Hung.:*** Tygacil; ***Indon.:*** Tygacil; ***Malaysia:*** Tygacil; ***Mex.:*** Tygacil; ***Pol.:*** Tygacil; ***Port.:*** Tygacil; ***UK:*** Tygacil; ***USA:*** Tygacil; ***Venez.:*** Tygacil.

Tilmicosin *(BAN, USAN, rINN)*

EL-870; LY-177370; Tilmicosina; Tilmicosine; Tilmicosinum. 4^A-*O*-De(2,6-dideoxy-3-*C*-methyl-α-L-*ribo*-hexopyranosyl)-20-deoxo-20-(*cis*-3,5-dimethyl-piperidino)tylosin.

Тильмикозин

$C_{46}H_{80}N_2O_{13}$ = 869.1.
CAS — 108050-54-0.
ATC Vet — QJ01FA91.



cis-form

Pharmacopoeias. In *US* for veterinary use only.
USP 31 (Tilmicosin). White to off-white amorphous solid. Slightly soluble in water and in *n*-hexane. Store at a temperature not exceeding 40°. Protect from light.

Tilmicosin Phosphate *(BANM, USAN, rINNM)*

Fosfato de tilmicosina; Tilmicosine, Phosphate de; Tilmicosini Phosphas.

Тильмикозина Фосфат

$C_{46}H_{80}N_2O_{13},H_3O_4P$ = 967.1.
CAS — 137330-13-3.

Profile

Tilmicosin is a macrolide antibacterial used as the base or the phosphate in veterinary medicine.

Adverse effects. Accidental self-injection of tilmicosin by a farm worker, resulting in asthenia and temporary pulmonary, gastrointestinal, and neuromuscular toxicity has been reported.[1] A review[2] of human exposures to tilmicosin injection reported between March 1992 and March 2005 suggested that the overall risk of serious adverse effects was about 2 cases per million doses. Serious cardiovascular adverse effects, including bradycardia, hypertension, hypotension, tachycardia, and tachypnoea, occurred in 156 of 3168 reported cases and, of these, fatalities occurred in 13.

1. Crown LA, Smith RB. Accidental veterinary antibiotic injection into a farm worker. *Tenn Med* 1999; **92:** 339–40.
2. Veenhuizen MF, *et al.* Analysis of reports of human exposure to Micotil 300 (tilmicosin injection). *J Am Vet Med Assoc* 2006; **229:** 1737–42.

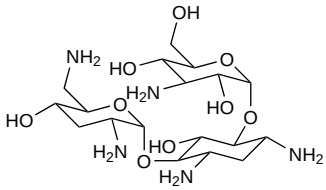
Handling. Contact with tilmicosin should be avoided. It is irritating to the eyes and may cause allergic reactions.

Tobramycin *(BAN, USAN, rINN)*

47663; Nebramycin Factor 6; Tobramicin; Tobramicina; Tobramicinas; Tobramisin; Tobramycine; Tobramycinum; Tobramycyna; Tobramysiini. 6-*O*-(3-Amino-3-deoxy-α-D-glucopyranosyl)-2-deoxy-4-*O*-(2,6-diamino-2,3,6-trideoxy-α-D-*ribo*-hexopyranosyl)streptamine.

Тобрамицин

$C_{18}H_{37}N_5O_9$ = 467.5.
CAS — 32986-56-4.
ATC — J01GB01; S01AA12.
ATC Vet — QJ01GB01; QS01AA12.



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Jpn*, and *US*.
Ph. Eur. 6.2 (Tobramycin). A substance produced by *Streptomyces tenebrarius* or obtained by any other means. A white or almost white powder. Freely soluble in water; very slightly soluble in alcohol. A 10% solution in water has a pH of 9.0 to 11.0.
USP 31 (Tobramycin). A white to off-white, hygroscopic powder. Freely soluble in water; very slightly soluble in alcohol; practically insoluble in chloroform and in ether. Contains not more than 8.0% w/w of water. A 10% solution in water has a pH of 9.0 to 11.0. Store in airtight containers.

Tobramycin Sulfate *(rINNM)*

Sulfato de tobramicina; Tobramycin Sulphate *(BANM)*; Tobramycine, Sulfate de; Tobramycini Sulfas; Tobramycyny siarczan.

Тобрамицина Сульфат

$(C_{18}H_{37}N_5O_9)_2,5H_2SO_4$ = 1425.4.
CAS — 49842-07-1 ($C_{18}H_{37}N_5O_9$,xH_2SO_4); 79645-27-5 ($(C_{18}H_{37}N_5O_9)_2,5H_2SO_4$).
ATC — J01GB01; S01AA12.
ATC Vet — QJ01GB01; QS01AA12.

Pharmacopoeias. In *Pol.* and *US*.
USP 31 (Tobramycin Sulfate). It has a potency of not less than 634 micrograms and not more than 739 micrograms of tobramycin per mg. A 4% solution in water has a pH of 6.0 to 8.0. Store in airtight containers.

Incompatibility. For discussion of the incompatibility of aminoglycosides, including tobramycin, with beta lactams, see under Gentamicin Sulfate, p.282. Tobramycin is also reported to be incompatible with various other drugs and, as injections have an acid pH, incompatibility with alkaline preparations or with drugs unstable at acid pH may reasonably be expected.

Adverse Effects, Treatment, and Precautions

As for Gentamicin Sulfate, p.282. Some studies suggest that tobramycin is slightly less nephrotoxic than gentamicin, but others have not found any significant difference in their effects on the kidneys.

Peak plasma-tobramycin concentrations greater than 12 micrograms/mL (the *BNF* suggests 10 micrograms/mL) and trough concentrations greater than 2 micrograms/mL should be avoided.

When tobramycin is given by inhalation with other inhaled drugs, they should be given first before the dose of tobramycin. After the first inhaled dose of tobramycin, patients should be monitored for bronchospasm and if it occurs, the test should be repeated using a bronchodilator. Peak flow should be measured before nebulisation and again after it. Caution should be exercised in the presence of severe haemoptysis. Renal function should be monitored before treatment and every six months during use.

Effects on the ear. Reversible vestibular toxicity (ataxia, dizziness, and oscillopsia) occurred in a patient on haemodialysis after about 3 weeks' treatment with inhaled tobramycin for bronchiectasis due to colonisation with *Pseudomonas aeruginosa*.[1]

1. Edson RS, *et al.* Vestibular toxicity due to inhaled tobramycin in a patient with renal insufficiency. *Mayo Clin Proc* 2004; **79:** 1185–91.

Effects on the kidney. Irreversible acute renal failure requiring haemodialysis occurred in a high-risk patient with chronic renal failure after being treated for 4 weeks with inhaled tobramycin for *Pseudomonas aeruginosa* pneumonia.[1]

1. Cannella CA, Wilkinson ST. Acute renal failure associated with inhaled tobramycin. *Am J Health-Syst Pharm* 2006; **63:** 1858–61.

Effects on the liver. A case of possible tobramycin-induced hepatotoxicity was reported in a 20-year-old patient receiving antibacterial treatment for *Pseudomonas aeruginosa* bacteraemia and osteomyelitis. Liver enzyme values started to increase when empirical treatment was changed to intravenous tobramycin and ceftazidime, and markedly increased when the regimen was changed, increasing the dose of tobramycin and replacing ceftazidime with piperacillin/tazobactam and then later aztreonam. Enzyme values began to decrease after all treatment was stopped on day 12.[1]

1. Nisly SA, *et al.* Tobramycin-induced hepatotoxicity. *Ann Pharmacother* 2007; **41:** 2061–5.

Interactions

As for Gentamicin Sulfate, p.283.

Antimicrobial Action

As for Gentamicin Sulfate, p.283. Tobramycin is reported to be somewhat more active *in vitro* than gentamicin against *Pseudomonas aeruginosa* and less active against *Serratia*, staphylococci, and enterococci; however these differences do not necessarily translate into differences in clinical effectiveness.

Cross-resistance between tobramycin and gentamicin is generally seen, but about 10% of strains resistant to gentamicin are susceptible to tobramycin.

◊ References to activity against *Pseudomonas aeruginosa*.

1. Barclay ML, *et al.* Adaptive resistance to tobramycin in Pseudomonas aeruginosa lung infection in cystic fibrosis. *J Antimicrob Chemother* 1996; **37:** 1155–64.
2. den Hollander JG, *et al.* Synergism between tobramycin and ceftazidime against a resistant Pseudomonas aeruginosa strain, tested in an in vitro pharmacokinetic model. *Antimicrob Agents Chemother* 1997; **41:** 95–100.
3. Wu YL, *et al.* Ability of azlocillin and tobramycin in combination to delay or prevent resistance development in Pseudomonas aeruginosa. *J Antimicrob Chemother* 1999; **44:** 389–92.
4. Shawar RM, *et al.* Activities of tobramycin and six other antibiotics against Pseudomonas aeruginosa isolates from patients with cystic fibrosis. *Antimicrob Agents Chemother* 1999; **43:** 2877–80.

Pharmacokinetics

As for Gentamicin Sulfate, p.284.

After intramuscular use of tobramycin, peak plasma concentrations are achieved within 30 to 90 minutes and concentrations of about 4 micrograms/mL have been reported following doses of 1 mg/kg. Usual doses by slow intravenous injection may result in plasma concentrations which briefly exceed 12 micrograms/mL. A plasma half-life of 2 to 3 hours has been reported. Sufficient tobramycin may be absorbed after inhalation to produce systemic adverse effects (see above).

Inhalation. References.

1. Touw DJ, *et al.* Pharmacokinetics of aerosolized tobramycin in adult patients with cystic fibrosis. *Antimicrob Agents Chemother* 1997; **41:** 184–7.
2. Beringer PM, *et al.* Pharmacokinetics of tobramycin in adults with cystic fibrosis: implications for once-daily administration. *Antimicrob Agents Chemother* 2000; **44:** 809–13.

Uses and Administration

Tobramycin is an aminoglycoside antibiotic with actions and uses similar to those of gentamicin (p.284). It is used, usually as the sulfate, particularly in the treatment of pseudomonal infections.

As with gentamicin, tobramycin may be used with penicillins or cephalosporins; the injections should be given separately.

Doses of tobramycin sulfate are expressed in terms of tobramycin base; 1.5 g of tobramycin sulfate is equivalent to about 1 g of tobramycin. Doses are similar to those of gentamicin, with the usual adult dose ranging from 3 to 5 mg/kg daily in 3 or 4 divided doses. In patients with cystic fibrosis, doses of 8 to 10 mg/kg daily in divided doses may be necessary to achieve therapeutic plasma concentrations.

The usual dose for children is 6 to 7.5 mg/kg daily in 3 or 4 divided doses. Premature and full-term neonates may be given 2 mg/kg every 12 hours.

For mild to moderate urinary-tract infections in adults, a dose of 2 to 3 mg/kg once daily may be effective. As with some other aminoglycosides, once-daily dosage has been used successfully in selected patients for the treatment of other infections without increasing toxicity but local guidelines should be consulted for dosage and serum concentrations (see also Once-daily Dosage, under Gentamicin, p.285).

Tobramycin sulfate is given by intramuscular injection, or by intravenous infusion over 20 to 60 minutes in 50 to 100 mL of sodium chloride 0.9% or glucose 5% injection; proportionately less fluid should be given to children. It has also been given slowly by direct intravenous injection.

Treatment should generally be limited to 7 to 10 days, and peak plasma concentrations greater than 12 micrograms/mL (the *BNF* suggests 10 micrograms/mL) or trough concentrations greater than 2 micrograms/mL should be avoided. In all patients, dosage should be adjusted according to plasma-tobramycin concentrations and particularly where factors such as age, renal impairment, or prolonged thera-

py may predispose to toxicity (see Uses and Administration of Gentamicin Sulfate, p.284).

Tobramycin may be used as a 0.3% eye ointment or eye drops in the treatment of eye infections. It is also given by inhalation in patients with cystic fibrosis to control *Pseudomonas aeruginosa* infections in a dose of 300 mg every 12 hours for 28 days using a suitable nebuliser. Treatment is then stopped for 28 days before being resumed for another treatment period. This cycle may be repeated indefinitely.

◊ Reviews.

1. Cheer SM, *et al.* Inhaled tobramycin (TOBI): a review of its use in the management of pseudomonas aeruginosa infections in patients with cystic fibrosis. *Drugs* 2003; **63:** 2501–20.

Preparations

BP 2008: Tobramycin Injection;
USP 31: Tobramycin and Dexamethasone Ophthalmic Ointment; Tobramycin and Dexamethasone Ophthalmic Suspension; Tobramycin and Fluorometholone Acetate Ophthalmic Suspension; Tobramycin for Injection; Tobramycin Inhalation Solution; Tobramycin Injection; Tobramycin Ophthalmic Ointment; Tobramycin Ophthalmic Solution.

Proprietary Preparations (details are given in Part 3)

Arg.: Bioptic; Fotex; Gotabiotic; Gotabiotic D; Klonamicin; Oftalbrax†; Radina; Tobi; Tobrabiotic; Tobradosa; Tobragan; Tobranet; Tobrex; Toflamixina; Tuberbut; Xao T; Xibrax; ***Austral.:*** Nebcin; Tobi; Tobrex; ***Austria:*** Brulamycin; Cromycin; Tobi; Tobrasix; Tobrex; ***Belg.:*** Obracin; Tobi; Tobrex; ***Braz.:*** Tobra-M†; Tobracin; Tobragan; Tobramina; Tobranom; Tobrex; Toflamixina†; ***Canad.:*** Nebcin†; Tobi; Tobrex; Tomycine†; ***Chile:*** Tobragan; Tobrex; Tobrin; Xolof; ***Cz.:*** Bramitob; Brulamycin; Tobi; Tobrex; ***Denm.:*** Nebcina; Tobi; Tobrex; ***Fin.:*** Nebcina†; Tobi; Tobrex; Tomycin; ***Fr.:*** Nebcine; Tobi; Tobrex; ***Ger.:*** Brulamycin†; Gernebcin; Tobi; Tobra-cell; Tobramaxin; ***Gr.:*** Colther; Eyebrex; Eyetobrin; Ikobel; Monobracin†; Monotobrin; Nebcin; Thilo-micine; Tobi; Tobrex; ***Hong Kong:*** Nebcin†; Tobrex; Toracin; ***Hung.:*** Brulamycin; Tobi; Tobrex; ***India:*** Ocutob; Tobacin; Tobazon; Tobraneg; ***Indon.:*** Bralifex; Dartobcin; Isotic Tobryne; Tobrex; Tobryne; ***Irl.:*** Nebcin†; Tobi; Tobralex†; ***Israel:*** Nebcin†; Tobi; Tobrex; ***Ital.:*** Bramicil; Bramitob; Nebicina; Tobi; Tobrabact; Tobral; Tobrastill; ***Malaysia:*** Tobrex; ***Mex.:*** Eyebrex; Micitrex; Obry; Tobra†; Tobrex; Trazil; Verbram; ***Neth.:*** Obracin; Tobi; Tobrabact; Tobrex; ***Norw.:*** Nebcina†; Tobi; Tobrex; ***NZ:*** Nebcin; Tobi†; Tobrex; ***Philipp.:*** Ramitop; Tobrex; ***Pol.:*** Tobi; Tobrex; Tobrosopt; ***Port.:*** Bramitob; Distobram†; Tobi; Tobra-Gobens; Tobrex; Tobrexan; Tobridavi; ***Rus.:*** Brulamycin (Бруламицин); Tobrex (Тобрекс); ***S.Afr.:*** Nebcin; Tobrex; ***Singapore:*** Tobrex; ***Spain:*** Tobi; Tobra Gobens; Tobrabact; Tobradistin†; Tobrex; Tobrexan; ***Swed.:*** Nebcina; Tobi; Tobrex; ***Switz.:*** Obracin; Tobi; Tobrex; ***Thai.:*** Tobrex; ***Turk.:*** Thilomaxine; Tobel; Tobrased; Tobrex; Tobsin; ***UK:*** Nebcin†; Tobi; ***USA:*** AkTob; Nebcin†; Tobi; Tobrasol; Tobrex; ***Venez.:*** Poentobral; Tobranax; Tobrasol; Tobrex; Trazil†.

Multi-ingredient: ***Arg.:*** Antibioptal; Bicrinol; Biocort; Bioptic DX; Decadron con Tobramicina; Fotadex; Gotabiotic F; Ingebrax; Klonamicin Compuesto; Larsen; Lotemicin; Polioftal; Radina Dex; Tobrabiotic D; Tobracort; Tobradex; Tobradiclo; Tobragan D; Tobratlas; Toflam; Toflamixina Plus; Xao-Dex†; Xibradex; ***Austria:*** Tobradex; ***Belg.:*** Ocubrax; Tobradex; ***Braz.:*** Tobracin D; Tobracort; Tobradex; ***Canad.:*** Tobradex; ***Chile:*** Poentobral Plus; Tobradex; Tobragan D; Tobrin-D; Todexona; Xolof D; ***Cz.:*** Tobradex; ***Fr.:*** Tobradex; ***Gr.:*** Dexamycin; Eyebrex-Dexa†; Lofoto; O-Biotic; Thilomicine Dex; Tobradex; Tobrafen; ***Hong Kong:*** Tobradex; ***Hung.:*** Ocubrax†; Tobradex; ***India:*** Obrasone; Ocutob-D; Tobazon DM; ***Indon.:*** Bralifex Plus; Isotic Tobrizon; Tobradex; ***Ital.:*** Tobradex; ***Malaysia:*** Tobradex; ***Mex.:*** Obrydex; Obrypre; Tobracort; Tobradex; Trazidex; Trazinac; ***Neth.:*** Tobradex; ***NZ:*** Tobradex; ***Philipp.:*** Tobradex; ***Pol.:*** Tobradex; ***Rus.:*** Tobradex (Тобрадекс); Tobrasone (Тобразон); ***S.Afr.:*** Tobradex; ***Singapore:*** Tobradex; ***Spain:*** Ocubrax; Tobradex; ***Switz.:*** Tobradex; Tobrafen; ***Thai.:*** Tobradex; ***Turk.:*** Ocubrax; ***UK:*** Tobradex; ***USA:*** Tobradex; ***Venez.:*** Poentobral Plus; Tobracort; Tobradex; Tobragan D; Todenac; Todex; Trazidex; Trazinac.

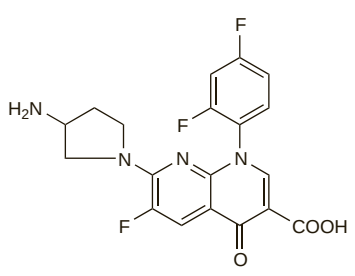
Tosufloxacin *(USAN, rINN)*

A-61827; Abbott-61827; Tosufloxacine; Tosufloxacino; Tosufloxacinum. (±)-7-(3-Amino-1-pyrrolidinyl)-1-(2,4-difluorophenyl)-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid.

Тосуфлоксацин

$C_{19}H_{15}F_3N_4O_3$ = 404.3.

CAS — 100490-36-6 (anhydrous tosufloxacin); 108138-46-1 (anhydrous tosufloxacin); 107097-79-0 (tosufloxacin monohydrate).



Tosufloxacin Tosilate *(rINNM)*

A-64730; T-3262; Tosilato de tosufloxacino; Tosufloxacin Tosylate; Tosufloxacine, Tosilate de; Tosufloxacini Tosilas. Tosufloxacin toluene-4-sulphonate monohydrate.

Тосуфлоксацина Тозилат

$C_{19}H_{15}F_3N_4O_3.C_7H_8O_3S.H_2O$ = 594.6.

CAS — 115964-29-9; 144742-63-2.

Profile

Tosufloxacin is a fluoroquinolone antibacterial with properties similar to those of ciprofloxacin (p.243). It is given orally as the tosilate in the treatment of susceptible infections in usual doses of 300 to 450 mg daily in 2 or 3 divided doses.

For blepharitis, conjunctivitis, corneal ulcers, and other eye infections caused by susceptible strains of bacteria, eye drops containing 0.3% of tosufloxacin tosilate are used.

Preparations

Proprietary Preparations (details are given in Part 3)
Jpn: Ozex.

Trimethoprim *(BAN, USAN, rINN)*

BW-56-72; NSC-106568; Triméthoprime; Trimethoprimum; Trimethoxyprim; Trimetopriimi; Trimetoprim; Trimetoprima; Trimetoprimas. 5-(3,4,5-Trimethoxybenzyl)pyrimidine-2,4-diamine.

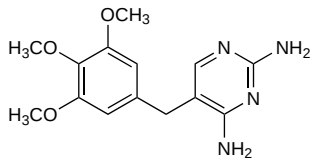
Триметоприм

$C_{14}H_{18}N_4O_3$ = 290.3.

CAS — 738-70-5.

ATC — J01EA01.

ATC Vet — QJ01EA01; QJ51EA01.



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

- Co-trifamole (*BAN*)—trimethoprim 1 part and sulfamoxole 5 parts (see p.257)
- Co-trimazine (*BAN*)—trimethoprim 1 part and sulfadiazine 5 parts (see p.258)
- Co-trimoxazole (*BAN*)—trimethoprim 1 part and sulfamethoxazole 5 parts (see p.258)
- Co-trimoxazole (*PEN*)—trimethoprim and sulfamethoxazole.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *US*, and *Viet.*
Ph. Eur. 6.2 (Trimethoprim). A white or yellowish-white powder. Very slightly soluble in water; slightly soluble in alcohol.
USP 31 (Trimethoprim). White to cream-coloured, odourless crystals or crystalline powder. Very slightly soluble in water; slightly soluble in alcohol and in acetone; soluble in benzyl alcohol; practically insoluble in carbon tetrachloride and in ether; sparingly soluble in chloroform and in methyl alcohol. Store in airtight containers. Protect from light.

Trimethoprim Sulfate *(USAN, rINNM)*

BW-72U; Sulfato de trimetoprima; Trimethoprim Sulphate *(BANM)*; Triméthoprime, Sulfate de; Trimethoprimi Sulfas; Trimetoprim Sülfat.

Триметоприма Сульфат

$(C_{14}H_{18}N_4O_3)_2.H_2SO_4$ = 678.7.

CAS — 56585-33-2.

Pharmacopoeias. In *Viet.* and *US.*
USP 31 (Trimethoprim Sulfate). A white to off-white crystalline powder. Soluble in water, in alcohol, in dilute mineral acids, and in fixed alkalis. pH of a 0.05% solution in water is between 7.5 and 8.5. Store at a temperature of 25°, excursions permitted between 15° and 30°.

Incompatibility. UK licensed product information states that trimethoprim injections (containing the lactate) should not be mixed with solutions of sulfonamides because of incompatibility. Although a former such preparation stated that it should not be diluted in chloride-containing infusion solutions, because of the risk of precipitating trimethoprim hydrochloride, others are stated to be compatible with sodium chloride 0.9% and some other chloride-containing solutions including Ringer's solution. Injections are considered compatible with glucose 5% and with sodium lactate.

Adverse Effects and Treatment

Trimethoprim is reasonably well tolerated in general, and the most frequent adverse effects at usual doses are pruritus and skin rash (in about 3 to 7% of patients) and mild gastrointestinal disturbances including nausea, vomiting, and glossitis.

Rarely, more severe effects have been reported. Sulfonamide-like skin reactions including exfoliative dermatitis, erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis have occurred. Disturbances of liver enzyme values and cholestatic jaundice have been associated with trimethoprim. Rises in serum creatinine and blood-urea nitrogen have been reported although it is unclear whether this represents genuine renal dysfunction or inhibition of tubular secretion of creatinine. Photosensitivity has been reported. Fever is not uncommon but occasionally hypersensitivity reactions may be severe and anaphylaxis and angioedema have been reported. Cases of aseptic meningitis have also occurred.

Trimethoprim may cause a depression of haematopoiesis due to interference of the drug in the metabolism of folic acid, particularly when given over a prolonged period or in high doses. This may manifest as megaloblastic anaemia, or as thrombocytopenia and leucopenia; methaemoglobinaemia has also been seen. Calcium folinate 5 to 15 mg daily by mouth may be given to counter this effect. Trimethoprim is teratogenic in *animals*.

For further information on the adverse effects of trimethoprim when used with sulfamethoxazole, see Co-trimoxazole, p.258.

Effects on the eyes. There have been isolated reports of bilateral anterior uveitis associated with trimethoprim. In 2 such patients,[1,2] the reaction recurred upon rechallenge with trimethoprim. A third patient developed uveitis after co-trimoxazole, and subsequently uveitis with retinal haemorrhage following trimethoprim alone.[3]

1. Gilroy N, *et al.* Trimethoprim-induced aseptic meningitis and uveitis. *Lancet* 1997; **350:** 112.
2. Arola O, *et al.* Arthritis, uveitis, and Stevens-Johnson syndrome induced by trimethoprim. *Lancet* 1998; **351:** 1102.
3. Kristinsson JK, *et al.* Bilateral anterior uveitis and retinal haemorrhages after administration of trimethoprim. *Acta Ophthalmol Scand* 1997; **75:** 314–15.

Hyperkalaemia. Trimethoprim has been reported to induce hyperkalaemia,[1] particularly in HIV-infected patients being treated for pneumocystis pneumonia or in the elderly. The hyperkalaemia may be due to amiloride-like potassium-sparing properties of trimethoprim, and may be potentiated by ACE inhibitors.

1. Perazella MA. Trimethoprim-induced hyperkalaemia: clinical data, mechanism, prevention and management. *Drug Safety* 2000; **22:** 227–36.

Precautions

Trimethoprim should not be given to patients with a history of hypersensitivity to the drug, and it should be stopped if a skin rash appears. Care is necessary in giving trimethoprim to patients with renal impairment to avoid accumulation and toxicity: it should not be given in severe renal impairment unless blood concentrations can be monitored. It should be used with caution in patients with severe hepatic damage as changes may occur in the absorption and metabolism of trimethoprim.

It is suggested that regular haematological examination should be made during prolonged courses of treatment although the *BNF* considers evidence of their practical value to be unsatisfactory; patients or their carers should be told how to recognise signs of blood toxicity and should be advised to seek immediate medical attention if symptoms such as fever, sore throat, rash, mouth ulcers, purpura, bruising or bleeding develop. Trimethoprim should not usually be given to patients with serious haematological disorders and particularly not in megaloblastic anaemia secondary to folate depletion. Care should be taken in patients with actual, or possible, folate deficiency and use of folinic acid should be considered. Trimethoprim should be avoided during pregnancy. Elderly patients may be more susceptible to adverse effects and a lower dosage may be advisable.

Trimethoprim may interfere with some diagnostic tests, including serum-methotrexate assay where dihydrofolate reductase is used and the Jaffé reaction for creatinine.