Sulfisomidine *(BAN, rINN)*

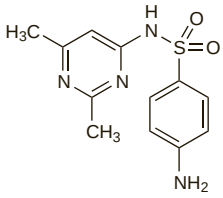
Sulfa-isodimérazine; Sulfaisodimidiini; Sulfaisodimidin; Sulfaisodimidine; Sulfaisodimidinum; Sulfasomidine; Sulfisomidiini; Sulfisomidin; Sulfisomidina; Sulfisomidinum; Sulfizomidinas; Sulphasomidine; Szulfizomidin. N^1-(2,6-Dimethylpyrimidin-4-yl)sulphanilamide.

Сульфизомидин

$C_{12}H_{14}N_4O_2S$ = 278.3.

CAS — 515-64-0.

ATC — J01EB01.



NOTE. Sulfadimethylpyrimidine has been used as a synonym for sulfisomidine, and sulphadimethylpyrimidine is sometimes used as a synonym for sulfadimidine (p.338). Care should be taken to avoid confusion between the two compounds, which are isomeric.

Pharmacopoeias. In *Eur.* (see p.vii).

Ph. Eur. 6.2 (Sulfisomidine). White or yellowish-white powder or crystals. Very slightly soluble in water; slightly soluble in alcohol and in acetone; dissolves in dilute solutions of alkali hydroxides and in dilute mineral acids. Protect from light.

Profile

Sulfisomidine is a short-acting sulfonamide with properties similar to those of sulfamethoxazole (p.340). It has been used topically for skin or vaginal infections and has also been given orally. The sodium salt has also been used.

Preparations

Proprietary Preparations (details are given in Part 3)
Thai.: Aristamed†.

Sultamicillin *(BAN, USAN, rINN)*

CP-49952; Sultamicilin; Sultamicilina; Sultamicilline; Sultamicillinum; Sultamisilin; Sultamisilliini; Sultamycylina. Penicillanoyloxymethyl (6*R*)-6-(D-2-phenylglycylamino)penicillanate *S*′,*S*′-dioxide.

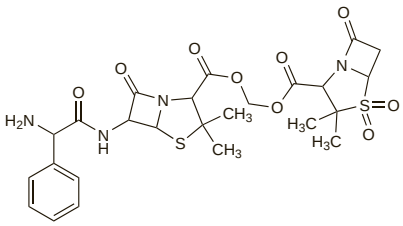
Сультамициллин

$C_{25}H_{30}N_4O_9S_2$ = 594.7.

CAS — 76497-13-7.

ATC — J01CR04.

ATC Vet — QJ01CR04.



Pharmacopoeias. In *Eur.* (see p.vii).

Ph. Eur. 6.2 (Sultamicillin). A semi-synthetic product derived from a fermentation product. A white or almost white, slightly hygroscopic, crystalline powder. Practically insoluble in water and in alcohol; very slightly soluble in methyl alcohol. Store in airtight containers.

Sultamicillin Tosilate *(BANM, rINNM)*

Sultamicilin-tosylát; Sultamicillin Tosylate; Sultamicilline, tosilate de; Sultamicillini tosilas; Sultamicillintosilat; Sultamisilliinitosilaatti; Sultamycyliny tozylan; Tosilato de sultamicilina. Sultamicillin toluene-4-sulphonate.

Сультамициллина Тозилат

$C_{25}H_{30}N_4O_9S_2,C_7H_8O_3S$ = 766.9.

CAS — 83105-70-8.

Pharmacopoeias. In *Chin.*
Eur. (see p.vii) and *Jpn* include the dihydrate.

Ph. Eur. 6.2 (Sultamicillin Tosilate Dihydrate; Sultamicillini Tosilas Dihydricus). A white or almost white, crystalline powder. Practically insoluble in water; sparingly soluble in alcohol. Store in airtight containers.

Profile

Sultamicillin is a prodrug of ampicillin (p.204) and of the beta-lactamase inhibitor sulbactam (p.335); it consists of the two compounds linked as a double ester. During absorption from the gastrointestinal tract it is hydrolysed, releasing equimolar quantities of ampicillin and sulbactam.

Sultamicillin is given orally as tablets containing sultamicillin tosilate or as oral suspension containing sultamicillin. It is used in the treatment of infections where beta-lactamase-producing organisms might occur, including uncomplicated gonorrhoea, otitis media, and respiratory-tract and urinary-tract infections. The usual dose is 375 to 750 mg of sultamicillin (equivalent to 147 to 294 mg of sulbactam and 220 to 440 mg of ampicillin) twice daily. A single dose of sultamicillin 2.25 g with probenecid 1 g may be used for uncomplicated gonorrhoea.

When parenteral therapy is necessary a combined preparation of ampicillin with sulbactam is given.

◊ References.

1. Friedel HA, *et al.* Sultamicillin: a review of its antibacterial activity, pharmacokinetic properties and therapeutic use. *Drugs* 1989; **37**: 491–522.
2. Lode H. Role of sultamicillin and ampicillin/sulbactam in the treatment of upper and lower bacterial respiratory tract infections. *Int J Antimicrob Agents* 2001; **18:** 199–209.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Ampigen SB; Unasyna; Unsayna†; ***Austria:*** Unasyn; ***Braz.:*** Unasyn; ***Chile:*** Unasyna; ***Ger.:*** Unacid PD; ***Gr.:*** Begalin; ***Hong Kong:*** Unasyn; ***Hung.:*** Unasyn; ***India:*** Sulbacin; ***Indon.:*** Bactesyn; Cinam; Picyn; Unasyn; Viccillin-SX; ***Ital.:*** Unasyn; ***Malaysia:*** Sulbacin; Unasyn; ***Mex.:*** Pentrexyl-S12-H; Unasyna; ***Philipp.:*** Unasyn; ***Pol.:*** Unasyn; ***Singapore:*** Unasyn; ***Spain:*** Unasyn†; ***Thai.:*** Combicid†; Sulam; Unasyn; ***Turk.:*** Alfasid; Ampisid; Combicid; Duobaktam; Duocid; Nobecid; Sulcid; Sultamat; Sultasid; Sultibac; ***Venez.:*** Fipexiam; Sinif; Sulamp; Sultamicina†; Sultamilan; Unasyn.

Multi-ingredient: ***Cz.:*** Unasyn.

Taurolidine *(BAN, rINN)*

Taurolidina; Taurolidinum. 4,4′-Methylenebis(perhydro-1,2,4-thiadiazine 1,1-dioxide).

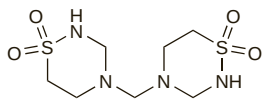
Тауролидин

$C_7H_{16}N_4O_4S_2$ = 284.4.

CAS — 19388-87-5.

ATC — B05CA05.

ATC Vet — QB05CA05.



Profile

Taurolidine is a broad-spectrum antibacterial. It is hydrolysed in aqueous solution to its monomeric form taurultam and other metabolites, with the release of what was originally thought to be formaldehyde but is now considered to be activated methylene glycol or methylol groups, from which it is believed to derive its activity. Its antibacterial activity *in vitro* is modest but is reported to be enhanced in the presence of serum or urine; it is active against pathogens including *Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas aeruginosa*. Taurolidine is also reported to inactivate bacterial endotoxin.

Taurolidine is used in peritonitis; a solution containing 0.5% is used for irrigation and another containing 2% is available for instillation. It has been given experimentally as an intravenous infusion in the treatment of severe sepsis or endotoxic shock and in pancreatitis.

Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Taurolin; ***Ger.:*** Taurolin; ***Neth.:*** Taurolin; ***Switz.:*** Taurolin.

Tazobactam Sodium *(BANM, USAN, rINNM)*

CL-307579; CL-298741 (tazobactam); Natrii Tazobactamum; Tazobactam sódico; Tazobactam sodique; Tazobactamum natricum; Tazobaktam Sodyum; YTR-830; YTR-830H (tazobactam). Sodium (2*S*,3*S*,5*R*)-3-methyl-7-oxo-3-(1*H*-1,2,3-triazol-1-ylmethyl)-4-thia-1-azabicyclo[3.2.0]-heptane-2-carboxylate 4,4-dioxide.

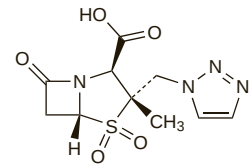
Натрий Тазобактам

$C_{10}H_{11}N_4NaO_5S$ = 322.3.

CAS — 89786-04-9 (tazobactam); 89785-84-2 (tazobactam sodium).

ATC — J01CG02.

ATC Vet — QJ01CG02.



(tazobactam)

Profile

Tazobactam is a penicillanic acid sulfone derivative with beta-lactamase inhibitory properties similar to those of sulbactam (p.335) although it is regarded as more potent. It has the potential to enhance the activity of beta-lactam antibacterials against beta-lactamase-producing bacteria.

Tazobactam sodium is given intravenously with piperacillin sodium (p.315) for the treatment of bacterial infections. The pharmacokinetics of tazobactam and piperacillin are similar.

◊ References.

1. Bush K, *et al.* Kinetic interactions of tazobactam with β-lactamases from all major structural classes. *Antimicrob Agents Chemother* 1993; **37:** 851–8.
2. Payne DJ, *et al.* Comparative activities of clavulanic acid, sulbactam, and tazobactam against clinically important β-lactamases. *Antimicrob Agents Chemother* 1994; **38:** 767–72.
3. Lee NLS, *et al.* β-Lactam antibiotic and β-lactamase inhibitor combinations. *JAMA* 2001; **285:** 386–8.

Preparations

Proprietary Preparations (details are given in Part 3)
Gr.: Zobactam; Zoracilin.

Multi-ingredient: ***Arg.:*** Pipetexina; Tazonam; ***Austral.:*** Tazocin; ***Austria:*** Tazonam; ***Belg.:*** Tazocin; ***Braz.:*** Tazocin; Tazoxil†; Tazpen†; ***Canad.:*** Tazocin; ***Chile:*** Tazonam; ***Cz.:*** Tazocin; ***Denm.:*** Tazocin; ***Fin.:*** Tazocin; ***Fr.:*** Tazocilline; ***Ger.:*** Tazobac; ***Gr.:*** Bactalin; Gramenox; Oliten; Tazepen; Tazidron; Tazobion; Tazocin; Tazorex; ***Hong Kong:*** Tazocin; ***Hung.:*** Tazocin; ***India:*** Dibact†; Tazact; Tazofast; Tazopen; Zosyn; ***Indon.:*** Tazocin; ***Irl.:*** Tazocin; ***Israel:*** Tazocin; ***Ital.:*** Tazobac; Tazocin; ***Malaysia:*** Tazocin; ***Mex.:*** Tasovak; Tazocin; ***Neth.:*** Tazocin; ***Norw.:*** Tazocin; ***NZ:*** Tazocin; ***Philipp.:*** Tazocin; ***Pol.:*** Tazocin; ***Port.:*** Tazobac; ***S.Afr.:*** Tazobax; Tazocin; ***Singapore:*** Tazocin; ***Spain:*** Tazocel; ***Swed.:*** Tazocin; ***Switz.:*** Tazobac; ***Thai.:*** Tazocin; ***Turk.:*** Tazocin; ***UK:*** Tazocin; ***USA:*** Zosyn; ***Venez.:*** Tazopril; Tazpen.

Teicoplanin *(BAN, USAN, rINN)*

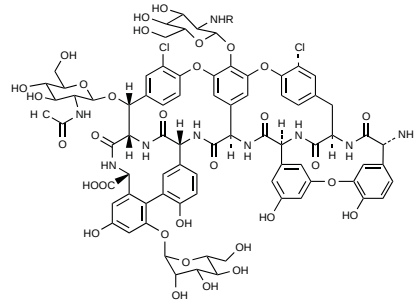
A-8327; DL-507-IT; L-12507; MDL-507; Teichomycin A_2; Teicoplanina; Téicoplanine; Teicoplaninum; Teikoplaniini; Teikoplanin.

Тейкопланин

CAS — 61036-62-2 (teichomycin); 61036-64-4 (teichomycin A_2).

ATC — J01XA02.

ATC Vet — QJ01XA02.



	R
Teicoplanin A -1	(*Z*)-4-decenoic acid
A -2	8-methylnonanoic acid
A -3	*n*-decanoic acid
A -4	8-methyldecanoic acid
A -5	9-methyldecanoic acid

Description. A glycopeptide antibiotic obtained from cultures of *Actinoplanes teichomyceticus* or the same substance obtained by any other means.

Pharmacopoeias. In *Jpn*.

Adverse Effects and Precautions

Fever, skin rash and pruritus, and occasional bronchospasm and anaphylaxis have been reported with teicoplanin, but, in comparison with vancomycin (p.359), it appears to be better tolerated when given by rapid intravenous injection and, although erythema and flushing of the upper body have occurred, the 'red-man syndrome' has been reported less often. In addition, unlike vancomycin, teicoplanin does not appear to cause tis-

sue necrosis and can be given by intramuscular injection. Other hypersensitivity reactions have included rigors, angioedema, and, rarely, severe skin reactions including exfoliative dermatitis, erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis.

Other reported reactions include gastrointestinal disturbances, dizziness, headache, thrombocytopenia (especially at high doses), leucopenia, neutropenia, eosinophilia, disturbances in liver enzyme values, and pain, erythema, and thrombophlebitis or abscess at the injection site. Rare cases of agranulocytosis have occurred. Renal impairment and ototoxicity have been reported but both appear to be less frequent than with vancomycin.

Renal and auditory function should be monitored during prolonged therapy in patients with pre-existing renal impairment, and in those receiving other ototoxic or nephrotoxic drugs, although opinions conflict as to whether increased risk of nephrotoxicity exists with combined therapy with drugs such as the aminoglycosides. In general, periodic blood counts and liver- and renal-function tests are advised during treatment.

No relationship has yet been established between plasma concentration and toxicity, and plasma-concentration monitoring is not generally considered necessary. Dosage adjustment is required in renal impairment.

Hypersensitivity. Although there have been occasional reports of cross-sensitivity to teicoplanin in patients hypersensitive to vancomycin,[1-4] the majority of reports suggest that cross-sensitivity is very rare and teicoplanin can usually be used in patients intolerant of vancomycin.[5-7]

1. McElrath MJ, *et al.* Allergic cross-reactivity of teicoplanin and vancomycin. *Lancet* 1986; **i:** 47.
2. Grek V, *et al.* Allergic cross-reaction of teicoplanin and vancomycin. *J Antimicrob Chemother* 1991; **28:** 476–7.
3. Marshall C, *et al.* Glycopeptide-induced vasculitis—cross-reactivity between vancomycin and teicoplanin. *J Infect* 1998; **37:** 82–3.
4. Kwon HS, *et al.* A case of hypersensitivity syndrome to both vancomycin and teicoplanin. *J Korean Med Sci* 2006; **21:** 1108–10.
5. Schlemmer B, *et al.* Teicoplanin for patients allergic to vancomycin. *N Engl J Med* 1988; **318:** 1127–8.
6. Smith SR, *et al.* Teicoplanin administration in patients experiencing reactions to vancomycin. *J Antimicrob Chemother* 1989; **23:** 810–12.
7. Wood G, Whitby M. Teicoplanin in patients who are allergic to vancomycin. *Med J Aust* 1989; **150:** 668.

Red-man syndrome. Although teicoplanin is believed[1,2] to be less likely than vancomycin to induce the red-man syndrome, symptoms consistent with the syndrome have nevertheless been reported after intravenous use.[3]

1. Sahai J, *et al.* Comparison of vancomycin- and teicoplanin-induced histamine release and "red man syndrome". *Antimicrob Agents Chemother* 1990; **34:** 765–9.
2. Rybak MJ, *et al.* Absence of "red man syndrome" in patients being treated with vancomycin or high-dose teicoplanin. *Antimicrob Agents Chemother* 1992; **36:** 1204–7.
3. Dubettier S, *et al.* Red man syndrome with teicoplanin. *Rev Infect Dis* 1991; **13:** 770.

Antimicrobial Action

As for Vancomycin Hydrochloride, p.359, although in general teicoplanin is more active against susceptible strains. In particular, it may be more active *in vitro* against enterococci and some anaerobic organisms, including strains of *Clostridium*. However, some coagulase-negative staphylococci are less sensitive to teicoplanin than to vancomycin.

Acquired resistance to teicoplanin has developed in staphylococci during treatment with teicoplanin. Cross-resistance with vancomycin has occurred in staphylococci and enterococci.

Pharmacokinetics

Teicoplanin is poorly absorbed from the gastrointestinal tract. After a 400-mg intravenous dose, peak plasma concentrations 1 hour later are reported to be in the range 20 to 50 micrograms/mL. It is well absorbed on intramuscular injection with a bioavailability of about 90%; after a dose of 3 mg/kg intramuscularly, peak plasma concentrations of 5 to 7 micrograms/mL have been reported after 2 to 4 hours.

The pharmacokinetics of teicoplanin are triphasic, with a biphasic distribution and a prolonged elimination. Penetration into the CSF is poor. It is taken up into white blood cells, and about 90 to 95% of teicoplanin in plasma is protein bound. It is excreted almost entirely by glomerular filtration in the urine, as unchanged drug. The terminal half-life is prolonged, but reported half-lives have ranged from about 30 to 190 hours or longer, depending on the sampling time; an effective clinical half-life of about 60 hours has been suggested for use in calculating dosage regimens. Half-life is increased progressively with increasing degrees of renal impairment. Teicoplanin is not removed by haemodialysis.

Teicoplanin is a mixture of several components, the pharmacokinetics of which have been shown to vary slightly, depending on their lipophilicity.

◊ Reviews.

1. Wilson APR. Clinical pharmacokinetics of teicoplanin. *Clin Pharmacokinet* 2000; **39:** 167–83.

Uses and Administration

Teicoplanin is a glycopeptide antibiotic that may be used as an alternative to vancomycin (p.360) in the treatment of serious Gram-positive infections where other drugs cannot be used, including the treatment and prophylaxis of infective endocarditis, peritonitis associated with continuous ambulatory peritoneal dialysis, and suspected infection in neutropenic or otherwise immunocompromised patients. Teicoplanin, given orally, has been suggested as a possible alternative to vancomycin or metronidazole in antibiotic-associated colitis. For details of these infections and their treatment, see under Choice of Antibacterial, p.162.

Teicoplanin is given intravenously, as a bolus dose or by infusion over 30 minutes, or by intramuscular injection. The usual mean dose is 6 mg/kg intravenously or intramuscularly initially, followed by 3 mg/kg intravenously or intramuscularly on each subsequent day of treatment (in practice this equates to a usual dose of 400 mg initially followed by 200 mg daily, except in patients weighing more than 85 kg in whom it is adapted accordingly). In more severe infections, 6 mg/kg may be given every 12 hours for the first 3 doses, followed by 6 mg/kg daily.

For the prophylaxis of endocarditis in high-risk patients undergoing dental or other procedures who are unable to receive penicillin, teicoplanin may be given in a single dose of 400 mg by intravenous injection, with gentamicin, before the procedure. A similar dose of teicoplanin is given for prophylaxis in orthopaedic surgery at induction of anaesthesia.

In children, a loading dose of 10 mg/kg every 12 hours for 3 doses is followed by 6 to 10 mg/kg daily, depending on the severity of infection. In neonates, a loading dose of 16 mg/kg on the first day is followed by maintenance doses of 8 mg/kg daily, given by intravenous infusion. Although no relationship between plasma concentrations and toxicity has been established, the *BNF* suggests that the former may sometimes be used as a guide to optimise treatment: trough concentrations should be above 10 micrograms/mL (15 to 20 micrograms/mL in patients with endocarditis) but less than 60 micrograms/mL.

Dosage should be adjusted in patients with impaired renal function (see Administration in Renal Impairment, below).

◊ Reviews.

1. Brogden RN, Peters DH. Teicoplanin: a reappraisal of its antimicrobial activity, pharmacokinetic properties and therapeutic efficacy. *Drugs* 1994; **47:** 823–54.
2. Murphy S, Pinney RJ. Teicoplanin or vancomycin in the treatment of Gram-positive infections? *J Clin Pharm Ther* 1995; **20:** 5–11.
3. de Lalla F, Tramarin A. A risk-benefit assessment of teicoplanin in the treatment of infections. *Drug Safety* 1995; **13:** 317–28.
4. Periti P, *et al.* Antimicrobial prophylaxis in orthopaedic surgery: the role of teicoplanin. *J Antimicrob Chemother* 1998; **41:** 329–40.
5. Schaison G, *et al.* Teicoplanin in the treatment of serious infection. *J Chemother* 2000; **12** (suppl 5): 26–33.

Administration in renal impairment. Doses of teicoplanin should be adjusted in patients with renal impairment, though reduction is not required until the fourth day of treatment. Teicoplanin should be given in usual doses for the first 3 days of therapy, thereafter the dose is adjusted according to creatinine clearance (CC):

- CC 40 to 60 mL/minute: half initial dose given daily or initial dose given every 2 days
- CC less than 40 mL/minute: one-third initial dose given daily or initial dose given every 3 days

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Targocid; Teicox; Teiklonal; Terbiox; ***Austral.:*** Targocid; ***Austria:*** Targocid; ***Belg.:*** Targocid; ***Braz.:*** Bactomax; Coplaxil†; Kirom; Targocid; Teicon; Teiconin†; Teicozid; ***Chile:*** Targocid; ***Cz.:*** Targocid; ***Denm.:*** Targocid; ***Fin.:*** Targocid; ***Fr.:*** Targocid; ***Ger.:*** Targocid; ***Gr.:*** Targocid; ***Hong Kong:*** Targocid; ***Hung.:*** Targocid; ***India:*** Targocid; Ticocin; ***Indon.:*** Targocid; ***Irl.:*** Targocid; ***Israel:*** Targocid; ***Ital.:*** Targosid; ***Jpn:*** Targocid; ***Malaysia:*** Targocid; ***Mex.:*** Targocid; Teripol; ***Neth.:*** Targocid; ***Norw.:*** Targocid; ***NZ:*** Targocid; ***Pol.:*** Targocid; ***Port.:*** Targosid; ***S.Afr.:*** Targocid; ***Singapore:*** Targocid; ***Spain:*** Targocid; ***Swed.:*** Targocid; ***Switz.:*** Targocid; ***Thai.:*** Targocid; ***Turk.:*** Targocid; ***UK:*** Targocid; ***Venez.:*** Targocid.

Multi-ingredient: ***Ger.:*** Targobone.

Telithromycin *(BAN, USAN, rINN)*

HMR-3647; RU-66647; Télithromycine; Telithromycinum; Telitromicina; Telitromisin. (3a*S*,4*R*,7*R*,9*R*,10*R*,11*R*,13*R*,15*R*,15a*R*)-4-Ethyloctahydro-11-methoxy-3a,7,9,11,13,15-hexamethyl-1-{4-[4-(3-pyridyl)imidazol-1-yl]butyl}-10-{[3,4,6-trideoxy-3-(dimethylamino)-β-D-*xylo*-hexopyranosyl]oxy}-2*H*-oxacyclotetradecino[4,3-*d*][1,3]oxazole-2,6,8,14(1*H*,7*H*,9*H*)-tetrone.

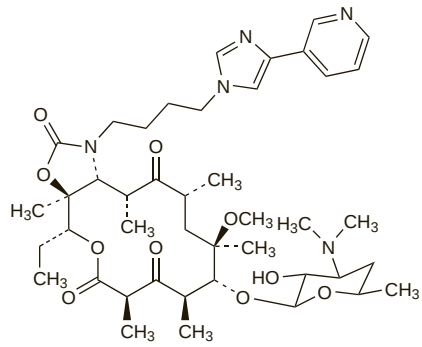
Телитромицин

$C_{43}H_{65}N_5O_{10}$ = 812.0.

CAS — 173838-31-8; 191114-48-4.

ATC — J01FA15.

ATC Vet — QJ01FA15.



Adverse Effects

Diarrhoea and other gastrointestinal disturbances such as nausea, vomiting, abdominal pain, and flatulence are among the most common adverse reactions after use of telithromycin. Severe, but usually reversible, hepatic dysfunction, including elevation of liver enzymes and hepatitis, with or without jaundice has been reported; however, there have been cases of fatal hepatotoxicity including fulminant hepatitis, hepatic necrosis, and hepatic failure. Effects on the CNS may include dizziness, headache, vertigo, and, occasionally, insomnia or drowsiness. Taste, and very rarely smell, disturbances may occur. Other less commonly reported adverse effects include paraesthesia, eosinophilia, skin rashes, and cardiovascular effects such as arrhythmias, hypotension, and bradycardia. Visual disturbances, particularly affecting accommodation, have occurred. Syncope, usually associated with the vagal syndrome, has been noted. Very rarely reported adverse effects include angioedema and anaphylaxis. There have been isolated cases of erythema multiforme, pseudomembranous colitis, and muscle cramps. Life-threatening acute respiratory failure has been reported in patients with myasthenia gravis (see also Precautions, below).

Effects on the eyes. Visual disturbances, namely blurred vision, difficulty with focusing, and diplopia have been associated with telithromycin. These have been reported to be more common in females under the age of 40 years and to occur in 1.1% of patients compared with 0.28% in those receiving a comparable antibacterial.[1] Licensed product information reports that symptoms are fully reversible, mostly mild to moderate in severity, and typically occur within a few hours of the first or second dose,