infants whose mothers had been given streptomycin during pregnancy. However, streptomycin is reported to be somewhat less nephrotoxic than the other aminoglycosides.

Paraesthesia in and around the mouth is not uncommon after intramuscular injection of streptomycin, and other neurological symptoms, including peripheral neuropathies, optic neuritis, and scotoma have occasionally occurred. Intrathecal use has resulted in symptoms of meningeal inflammation including radiculitis, arachnoiditis, nerve root pain, and paraplegia, and some recommend that it be avoided. The risk of neurotoxic reactions is greater in patients with renal impairment or pre-renal azotaemia.

Hypersensitivity skin reactions are reported in about 5% of patients, and eosinophilia may occur. There have been reports of Stevens-Johnson syndrome, toxic epidermal necrolysis, severe exfoliative dermatitis, and anaphylaxis. Sensitisation is common among those who handle streptomycin occupationally. Topical and inhalational use of streptomycin should be avoided. If necessary, hypersensitivity can usually be overcome by desensitisation. Aplastic anaemia and agranulocytosis have been reported rarely.

Although sources differ, it is usually suggested that peak plasma concentrations should be between 15 and 40 micrograms/mL, and trough concentrations below 3 to 5 micrograms/mL; in the UK the *BNF* recommends that trough concentrations in excess of 1 microgram/mL should be avoided in those over 50 years of age or those with renal impairment. A total cumulative dose in excess of 100 g may be associated with a higher incidence of adverse effects and should only be exceeded in exceptional circumstances.

Breast feeding. No adverse effects have been seen in breast-fed infants whose mothers were receiving streptomycin, and the American Academy of Pediatrics considers[1] that it is therefore usually compatible with 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 28/05/04)

Handling. Streptomycin may cause severe dermatitis in sensitised persons, and pharmacists, nurses, and others who handle the drug frequently should wear masks and rubber gloves.

Interactions

As for Gentamicin Sulfate, p.283.

Antimicrobial Action

Streptomycin has a mode of action and antimicrobial spectrum similar to that of gentamicin (p.283), although most strains of *Pseudomonas aeruginosa* are resistant. It is effective against *Yersinia pestis, Francisella tularensis*, and *Brucella* spp. Streptomycin has particular activity against *Mycobacterium tuberculosis*.

Resistance to streptomycin has often been reported and may develop in strains which are initially sensitive within a few days or weeks of beginning therapy. The widespread emergence of resistance has largely halted its use in infections due to the common Gram-negative aerobes. Primary resistance in *M. tuberculosis* is relatively uncommon in the UK and USA but may be seen in a third or more of cases in the Far East.

Both low-level and high-level resistance have been reported; the latter is thought to be due to mutation of the ribosomal binding site of the antibiotic and cannot be overcome by the synergistic use of another drug such as a beta lactam, whereas strains with moderate resistance due to decreased uptake or permeability of streptomycin may respond to combined use.

Organisms resistant to framycetin, kanamycin, neomycin, and paromomycin usually show cross-resistance to streptomycin, although streptomycin-resistant strains sometimes respond to one of these drugs.

◊ References.

1. Cooksey RC, *et al.* Characterization of streptomycin resistance mechanisms among Mycobacterium tuberculosis isolates from patients in New York City. *Antimicrob Agents Chemother* 1996; **40:** 1186–8.
2. Ho YII, *et al.* In-vitro activities of aminoglycoside-aminocyclitols against mycobacteria. *J Antimicrob Chemother* 1997; **40:** 27–32.

Pharmacokinetics

As for Gentamicin Sulfate, p.284. After intramuscular injection of streptomycin, maximum concentration in the blood is reached in 0.5 to 2 hours but the time taken and the concentration attained, which may be as high as about 50 micrograms/mL after a dose of 1 g, vary considerably. The half-life of streptomycin is about 2.5 hours. About one-third of streptomycin in the circulation is bound to plasma proteins. It is rapidly excreted by glomerular filtration and the concentration of streptomycin in the urine is often very high, with about 30 to 90% of a dose usually being excreted within 24 hours. It is distributed into breast milk.

Uses and Administration

Streptomycin is an aminoglycoside antibacterial mainly used as a first-line drug, with other antimycobacterials, in the treatment of tuberculosis. It is given during the initial phase of treatment unless the risk of drug resistance is small. Streptomycin has been used, with a penicillin, as an alternative to gentamicin in the treatment of bacterial endocarditis. Streptomycin is effective in the treatment of plague, tularaemia, and, with a tetracycline, in brucellosis. It has also been used, with other drugs, in various other infections including mycetoma and Whipple's disease. For details of these infections and their treatment, see under Choice of Antibacterial, p.162.

Streptomycin is mostly used as the sulfate but doses are expressed in terms of the base; 1.25 g of streptomycin sulfate is equivalent to about 1 g of streptomycin. It is given by intramuscular injection.

In the treatment of tuberculosis, streptomycin is given during the initial phase of short-course regimens in usual adult doses of 15 mg/kg daily, up to a maximum of 1 g daily. The maximum daily dose should be reduced to 500 to 750 mg in adults aged over 40 years, and in those weighing less than 50 kg. Dosage should also be reduced in those with renal impairment, in whom plasma-drug concentration should be monitored. Streptomycin may also be given as part of an intermittent regimen 2 or 3 times weekly. It has been given by the intrathecal route, together with intramuscular dosage, for tuberculous meningitis, but this is no longer recommended.

Children and infants aged 1 month to 18 years with tuberculosis may be given streptomycin 20 to 40 mg/kg daily (to a maximum of 1 g daily).

In the treatment of non-tuberculous infections, streptomycin has been given in usual adult doses of 1 to 2 g daily in divided doses, depending on the susceptibility and severity of infection; children may be given 20 to 40 mg/kg daily (maximum 1 g daily), usually in 2 to 4 divided doses.

In all patients dosage should preferably be adjusted according to plasma-streptomycin concentrations, and particularly where factors such as age, renal impairment, or prolonged therapy may predispose to toxicity. The course of treatment (other than in tuberculosis) should usually be limited to 7 to 14 days, and peak plasma concentrations should be between 15 and 40 micrograms/mL and trough concentrations below 3 to 5 micrograms/mL or below 1 microgram/mL in renal impairment or in those over 50 years of age. For discussion of the methods used to calculate aminoglycoside dosage requirements, see under Gentamicin Sulfate, p.284.

Streptomycin has also been used as the hydrochloride, the pantothenate, and as a complex with calcium chloride.

Administration and dosage. A report of the successful use of streptomycin 7 to 15 mg/kg as an intravenous infusion over 30 to 60 minutes in 4 patients with tuberculosis. Despite the view that streptomycin should be given intramuscularly because of the greater risk of toxicity with the intravenous route, this study was considered to indicate that intravenous use was feasible in selected patients unable to tolerate the intramuscular route.[1]

1. Driver AG, Worden JP. Intravenous streptomycin. *DICP Ann Pharmacother* 1990; **24:** 826–8.

Ménière's disease. Streptomycin and gentamicin have been used for medical ablation in advanced Ménière's disease (p.564). Systemic treatment has generally been limited by the development of chronic ataxia and oscillopsia (oscillating vision). However, streptomycin sulfate 1 g twice daily by intramuscular injection on 5 days each week for 2 weeks, repeated as necessary to a total dose of up to 60 g,[1,2] or 1 g twice daily for 5 days, followed if necessary by a further 3 days of treatment in the second week,[3] has produced improvements in vestibular symptoms without hearing loss in patients with Ménière's disease. Local (intratympanic) injections have also been tried,[4] but gentamicin is considered to be less toxic and is now generally preferred.

1. Shea JJ, *et al.* Long-term results of low dose intramuscular streptomycin for Ménière's disease. *Am J Otol* 1994; **15:** 540–4.
2. Balyan FR, *et al.* Titration streptomycin therapy in Meniere's disease: long-term results. *Otolaryngol Head Neck Surg* 1998; **118:** 261–6.
3. Graham MD. Bilateral Meniere's disease: treatment with intramuscular titration streptomycin sulfate. *Otolaryngol Clin North Am* 1997; **30:** 1097–1100.
4. Beck C, Schmidt CL. 10 Years of experience with intratympanally applied streptomycin (gentamycin) in the therapy of Morbus Menière. *Arch Otorhinolaryngol* 1978; **221:** 149–52.

Preparations

BP 2008: Streptomycin Injection;
USP 31: Streptomycin for Injection; Streptomycin Injection.

Proprietary Preparations (details are given in Part 3)

Cz.: Strepto-Fatol; ***Ger.:*** Strepto-Fatol; Strepto-Hefa; ***Gr.:*** Pan-Streptomycin†; ***India:*** Ambistryn-S; Cipstryn; ***Mex.:*** Bucomicina; Sulfestrep; ***S.Afr.:*** Bio-Strep; Novostrep†; Solustrep; ***Thai.:*** Strepto.

Multi-ingredient: ***Arg.:*** Estreptocarbocaftiazol; ***Braz.:*** Ortocilin†; ***India:*** Strepto-Erbazide†; ***Mex.:*** Aguipental; ***Port.:*** Bienterico.

Succinylsulfathiazole *(BAN, rINN)*

Succinilsolfatiazolo; Succinilsulfatiazol; Succinylsulfathiazol; Succinylsulfathiazolum; Succinylsulfathiazolum Monohydricum; Succinylsulfatiazol; Succinylsulphathiazole; Sukcinilsulfatiazolas; Sukcinylsulfathiazol monohydrát; Suksinyylisulfatiatsoli; Szukcinilszulfatiazol. 4′-(1,3-Thiazol-2-ylsulphamoyl)succinanilic acid monohydrate.

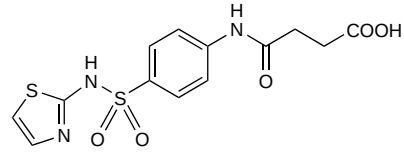
Сукцинилсульфатиазол

$C_{13}H_{13}N_3O_5S_2,H_2O$ = 373.4.

CAS — 116-43-8 (anhydrous succinylsulfathiazole).

ATC — A07AB04.

ATC Vet — QA07AB04.



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

Ph. Eur. 6.2 (Succinylsulfathiazole). A white or yellowish-white crystalline powder. Very slightly soluble in water; slightly soluble in acetone and in alcohol; dissolves in solutions of alkali hydroxides and carbonates. Protect from light.

Profile

Succinylsulfathiazole is a sulfonamide with properties similar to those of sulfamethoxazole (p.340). It is poorly absorbed and has been given for its antibacterial activity in the gastrointestinal tract.

Preparations

Proprietary Preparations (details are given in Part 3)

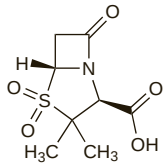
Multi-ingredient: ***Venez.:*** Guanicar.

Sulbactam *(BAN, rINN)*

CP-45899; Sulbactamum; Sulbaktaami; Sulbaktam. Penicillanic acid 1,1-dioxide; (2*S*,5*R*)-3,3-Dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid 4,4-dioxide.

Сульбактам

$C_8H_{11}NO_5S$ = 233.2.
CAS — 68373-14-8.
ATC — J01CG01.
ATC Vet — QJ01CG01.



Sulbactam Sodium *(BANM, USAN, rINNM)*

CP-45899-2; Natrii Sulbactamum; Sulbactam sódico; Sulbactam sodique; Sulbactamum natricum; Sulbaktaaminatrium; Sulbaktam sodná sůl; Sulbaktam sodowy; Sulbaktamnatrium.

Натрий Сульбактам

$C_8H_{10}NNaO_5S$ = 255.2.
CAS — 69388-84-7.
ATC — J01CG01.
ATC Vet — QJ01CG01.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Jpn*, and *US*.
Ph. Eur. 6.2 (Sulbactam Sodium). A white or almost white, hygroscopic, crystalline powder. Freely soluble in water; very slightly soluble in alcohol; sparingly soluble in ethyl acetate. It is freely soluble in diluted acids. A 5.0% solution in water has a pH of 4.5 to 7.2; if the substance is sterile: 5.2 to 7.2. Store in airtight containers.
USP 31 (Sulbactam Sodium). A white to off-white crystalline powder. It contains not less than 886 micrograms and not more than 941 microgram of sulbactam per mg, calculated on the anhydrous basis. Freely soluble in water and in dilute acid; sparingly soluble in acetone, in chloroform, and in ethyl acetate. Store in airtight containers.

Pivsulbactam *(BAN)*

CP-47904; Sulbactam Pivoxil *(USAN)*. Pivaloyloxymethyl penicillanate 1,1-dioxide.

Пивсульбактам

$C_{14}H_{21}NO_7S$ = 347.4.
CAS — 69388-79-0.

Profile
Sulbactam is a penicillanic acid sulfone with beta-lactamase inhibitory properties. It is active against Neisseriaceae and *Acinetobacter baumanii*, but generally has only weak antibacterial activity against other organisms. It is an irreversible inhibitor of many plasmid-mediated and some chromosomal beta-lactamases and has a similar spectrum of beta-lactamase inhibition to clavulanic acid (p.250), although it is regarded as less potent. Sulbactam can therefore enhance the activity of penicillins and cephalosporins against many resistant strains of bacteria.

It is given with ampicillin (p.204) in the treatment of infections where beta-lactamase production is suspected. Sulbactam is poorly absorbed from the gastrointestinal tract and is given by injection as the sodium salt. The pharmacokinetics of parenteral sulbactam and ampicillin are similar. For oral use the mutual prodrug sultamicillin (p.344) is available in some countries. Sulbactam is also given orally as the pivoxil derivative, pivsulbactam, with amoxicillin. Sulbactam has also been given with cefoperazone.

◊ References.

1. Campoli-Richards DM, Brogden RN. Sulbactam/ampicillin: a review of its antibacterial activity, pharmacokinetic properties, and therapeutic use. *Drugs* 1987; **33:** 577–609.
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. Nicolas-Chanoine MH. Inhibitor-resistant β-lactamases. *J Antimicrob Chemother* 1997; **40:** 1–3.
4. Lee NLS, *et al.* β-Lactam antibiotic and β-lactamase inhibitor combinations. *JAMA* 2001; **285:** 386–8.
5. 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.
6. Kanra G. Experience with ampicillin/sulbactam in severe infections. *J Int Med Res* 2002; **30** (suppl 1): 20A–30A.
7. Rafailidis PI, *et al.* Ampicillin/sulbactam: current status in severe bacterial infections. *Drugs* 2007; **67:** 1829–49.
8. Akova M. Sulbactam-containing beta-lactamase inhibitor combinations. *Clin Microbiol Infect* 2008; **14** (suppl 1): 185–8.

Breast feeding. Although sulbactam is distributed into breast milk in small amounts,[1] no adverse effects have been seen in breast-fed infants and the American Academy of Pediatrics considers that it is usually compatible with breast feeding.[2]

1. Foulds G, *et al.* Sulbactam kinetics and excretion into breast milk in postpartum women. *Clin Pharmacol Ther* 1985; **38:** 692–6.
2. 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 28/05/04)

Preparations
USP 31: Ampicillin and Sulbactam for Injection.

Proprietary Preparations (details are given in Part 3)
Austria: Combactam; ***Ger.:*** Combactam; ***Turk.:*** Ampisid.

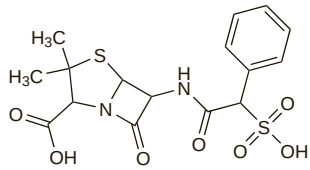
Multi-ingredient: ***Arg.:*** Aminoxidin Sulbactam; Ampi-Bis Plus; Ampigen SB; Darzitil SB; Prixin; Sulperazon†; Trifamox IBL; Unasyna; Unsayna†; ***Austria:*** Unasyn; ***Braz.:*** Combactan; Sulbacter†; Sulbamox; Trifamox; Unasyn; ***Chile:*** Sulbamox; Sulperazon; Unasyn; ***Cz.:*** Sulperazon; Unasyn; ***Fr.:*** Unacim; ***Ger.:*** Unacid; ***Gr.:*** Begalin-P; ***Hong Kong:*** Sulperazon; Unasyn; ***Hung.:*** Unasyn; ***India:*** Keftragard; Lactagard; Sulbacef; Sulbacin; Sultax; Zosul; ***Indon.:*** Fosular; Stabactam; Sulperazon; ***Israel:*** Unasyn; ***Ital.:*** Bethacil; Loricin; Unasyn; ***Jpn:*** Sulperazon†; Unasyn-S†; ***Malaysia:*** Sulbacin; Sulperazon; Unasyn; ***Mex.:*** Megamox; Trifamox IBL; Unasyna; ***Philipp.:*** Sulperazone; Unasyn; ***Pol.:*** Sulperazon; Unasyn; ***Rus.:*** Sulcef (Сульцеф); Sulperason (Сульперазон); Sultasin (Сультасин); Trifamox IBL (Трифамокс ИБЛ); Unasyn (Уназин); ***Singapore:*** Unasyn; ***Spain:*** Unasyn; ***Thai.:*** Cebactam; Cefper; Sulam; Sulcef; Sulperazon; Unasyn; ***Turk.:*** Combicid; Duobak; Duobaktam; Duocid; Nobecid; Primasef; Sulbaksit; Sulcid; Sulperazon; Sultasid; ***USA:*** Unasyn; ***Venez.:*** Ampibactan; Ampitren†; Fipexiam; Sinif; Sulperazon; Unasyn.

Sulbenicillin Sodium *(rINNM)*

Natrii Sulbenicillinum; Sulbenicilina sódica; Sulbénicilline Sodique; α-Sulfobenzylpenicillin Sodium; Sulfocillin Sodium. The disodium salt of (6*R*)-6-(2-phenyl-2-sulphoacetamido)penicillanic acid.

Натрий Сульбеницеллин

$C_{16}H_{16}N_2Na_2O_7S_2$ = 458.4.
CAS — 34779-28-7 (sulbenicillin); 41744-40-5 (sulbenicillin).
ATC — J01CA16.
ATC Vet — QJ01CA16.



(sulbenicillin)

Pharmacopoeias. In *Chin.* and *Jpn.*

Profile
Sulbenicillin sodium has actions and uses similar to those of carbenicillin sodium (p.216). It is given by intramuscular or intravenous injection or infusion.

Preparations
Proprietary Preparations (details are given in Part 3)
Indon.: Kedacillin; ***Jpn:*** Lilacillin†; ***Mex.:*** Kedacillin; ***Philipp.:*** Kedacillin.

Sulfabenzamide *(BAN, USAN, rINN)*

Sulfabensamid; Sulfabentsamidi; Sulfabenzamida; Sulfabenzamidum. *N*-Sulphanilylbenzamide.

Сульфабензамид

$C_{13}H_{12}N_2O_3S$ = 276.3.
CAS — 127-71-9.

Pharmacopoeias. In *US*.
USP 31 (Sulfabenzamide). A fine, white, practically odourless powder. Insoluble in water and in ether; soluble in alcohol, in acetone, and in sodium hydroxide 4% solution. Protect from light.

Profile
Sulfabenzamide is a sulfonamide with properties similar to those of sulfamethoxazole (p.340). It is reported to exert an optimal bacteriostatic action at pH 4.6. It is used with sulfacetamide and sulfathiazole in pessaries or a vaginal cream for the treatment of bacterial vaginosis, although its value has been questioned. The vaginal cream has also been used for the prevention of bacterial infection after cervical and vaginal surgery.

Preparations
USP 31: Triple Sulfa Vaginal Cream; Triple Sulfa Vaginal Tablets.

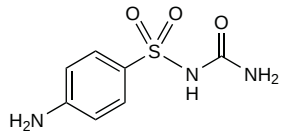
Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Belg.:*** Sultrin†; ***Braz.:*** Vagi-Sulfa; ***Gr.:*** Sultrin; ***Irl.:*** Sultrin†; ***Philipp.:*** Sultrin; ***Port.:*** Sultrin†; ***S.Afr.:*** Sultrin; ***UK:*** Sultrin†; ***USA:*** Sultrin.

Sulfacarbamide *(BAN, rINN)*

Sulfacarbamida; Sulfacarbamidum; Sulfakarbamid; Sulfanilcarbamide; Sulfaurea; Sulphacarbamide; Sulphanilylurea; Sulphaurea; Urosulphanum. Sulphanilylurea monohydrate.

Сульфакарбамид

$C_7H_9N_3O_3S,H_2O$ = 233.2.
CAS — 547-44-4 (anhydrous sulfacarbamide); 6101-35-5 (sulfacarbamide monohydrate).



Pharmacopoeias. In *Pol*.

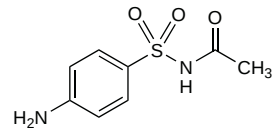
Profile
Sulfacarbamide is a sulfonamide with properties similar to those of sulfamethoxazole (p.340). It has been used in the treatment of urinary-tract infections, sometimes with other drugs.

Sulfacetamide *(BAN, rINN)*

Acetosulfaminum; Sulfacetamid; Sulfacetamida; Sulfacétamide; Sulfacetamidum; Sulfatsetamidi; Sulphacetamide. *N*-Sulphaniloylacetamide.

Сульфацетамид

$C_8H_{10}N_2O_3S$ = 214.2.
CAS — 144-80-9.
ATC — S01AB04.
ATC Vet — QS01AB04.



Pharmacopoeias. In *Int.* and *US*.
USP 31 (Sulfacetamide). A white, odourless, crystalline powder. Slightly soluble in water and in ether; soluble in alcohol; very slightly soluble in chloroform; freely soluble in dilute mineral acids and in solutions of potassium and sodium hydroxides; practically insoluble in benzene. Solutions in water are acid to litmus and sensitive to light; they are unstable when acidic or strongly alkaline. Protect from light.

Sulfacetamide Sodium *(BANM, rINNM)*

Natrii Sulfacetamidum; Soluble Sulphacetamide; Sulfacetamid sodná sůl monohydrát; Sulfacetamid sodowy; Sulfacetamida sódica; Sulfacétamide sodique; Sulfacetamidnatrium; Sulfacetamido natrio druska; Sulfacetamidum natricum; Sulfacetamidum Natricum Monohydricum; Sulfacylum; Sülfasetamid Sodyum; Sulfasetamidinatrium; Sulphacetamide Sodium; Sulphacetamidum Sodium; Szulfacetamid-nátrium.

Натрий Сульфацетамид

$C_8H_9N_2NaO_3S,H_2O$ = 254.2.
CAS — 127-56-0 (anhydrous sulfacetamide sodium); 6209-17-2 (sulfacetamide sodium monohydrate).
ATC — S01AB04.
ATC Vet — QS01AB04.

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

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *US*, and *Viet.*
Ph. Eur. 6.2 (Sulfacetamide Sodium). A white or yellowish-white, crystalline powder. Freely soluble in water; slightly soluble in dehydrated alcohol. A 5% solution in water has a pH of 8.0 to 9.5. Protect from light.
USP 31 (Sulfacetamide Sodium). A white odourless crystalline powder. Soluble 1 in 2.5 of water; sparingly soluble in alcohol; practically insoluble in chloroform and in ether. A 5% solution in water has a pH of 8.0 to 9.5. Store in airtight containers. Protect from light.

Stability. When solutions of sulfacetamide sodium are heated, hydrolysis occurs forming sulfanilamide which may be deposited as crystals, especially from concentrated solutions and under cold storage conditions.

Adverse Effects, Treatment, and Precautions
As for Sulfamethoxazole, p.340.
Local application of sulfacetamide sodium to the eye may cause burning or stinging but this is rarely severe enough to require stopping treatment.