Sisomicin Sulfate *(USAN, rINNM)*

Antibiotic 6640 (sisomicin); Rickamicin Sulphate; Sch-13475 (sisomicin); Sisomicin Sulphate *(BANM)*; Sisomicine, Sulfate de; Sisomicini Sulfas; Sissomicin Sulphate; Sulfato de sisomicina. 4-*O*-[(2*R*,3*R*)-*cis*-3-Amino-6-aminomethyl-3,4-dihydro-2*H*-pyran-2-yl]-2-deoxy-6-*O*-(3-deoxy-4-*C*-methyl-3-methylamino-β-L-arabinopyranosyl)streptamine sulphate; 2-Deoxy-6-*O*-(3-deoxy-4-*C*-methyl-3-methylamino-β-L-arabinopyranosyl)-4-*O*-(2,6-diamino-2,3,4,6-tetradeoxy-D-*glycero*-hex-4-enopyranosyl)streptamine sulphate.

Сизомицина Сульфат

$(C_{19}H_{37}N_5O_7)_2,5H_2SO_4$ = 1385.4.

CAS — 32385-11-8 (sisomicin); 53179-09-2 (sisomicin sulfate).

ATC — J01GB08.

ATC Vet — QJ01GB08.

Pharmacopoeias. In *Chin.*, *Jpn*, and *US*.

USP 31 (Sisomicin Sulfate). It loses not more than 15% of its weight on drying. 1 mg of sisomicin sulfate has a potency equivalent to not less than 580 micrograms of sisomicin calculated on the dried basis. A 4% solution in water of sisomicin has a pH of 3.5 to 5.5. Store in airtight containers.

Profile

Sisomicin, an antibiotic produced by *Micromonospora inyoensis* and closely related to gentamicin C_{1A}, is an aminoglycoside with general properties similar to those of gentamicin (p.282). It is given as the sulfate but doses are expressed in terms of the base; 1.5 g of sisomicin sulfate is equivalent to about 1 g of sisomicin. The usual dose for adults is 3 mg/kg daily given intramuscularly in 2 or 3 divided doses. It may be given by intravenous infusion if necessary.

Preparations

USP 31: Sisomicin Sulfate Injection.

Proprietary Preparations (details are given in Part 3)
India: Sisoptin; ***Ital.:*** Mensiso†.

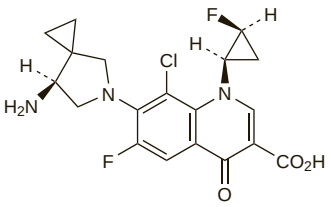
Sitafloxacin *(USAN, rINN)*

DU-6859 (anhydrous sitafloxacin); DU-6859a (sitafloxacin sesquihydrate); Sitafloxacine; Sitafloxacino; Sitafloxacinum. (–)-7-[(7*S*)-7-Amino-5-azaspiro[2.4]hept-5-yl]-8-chloro-6-fluoro-1-[(1*R*,2*S*)-2-fluorocyclopropyl]-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid.

Ситафлоксацин

$C_{19}H_{18}ClF_2N_3O_3$ = 409.8.

CAS — 127254-12-0 (anhydrous sitafloxacin); 163253-37-0 (sitafloxacin monohydrate); 163253-35-8 (sitafloxacin sesquihydrate).



NOTE. Sitafloxacin exists in several hydration states; the name sitafloxacin has been used to refer to both the anhydrous substance and the sesquihydrate ($C_{19}H_{18}ClF_2N_3O_3,1/H_2O$ = 436.8); the latter is known in Japan as sitafloxacin hydrate.

Profile

Sitafloxacin is a fluoroquinolone that is given orally in the treatment of susceptible infections.

Preparations

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

Sparfloxacin *(BAN, USAN, rINN)*

AT-4140; CI-978; Esparfloxacino; PD-131501; RP-64206; Sparfloksasiini; Sparfloxacine; Sparfloxacinum. 5-Amino-1-cyclopropyl-7-(*cis*-3,5-dimethylpiperazin-1-yl)-6,8-difluoro-1,4-dihydro-4-oxoquinoline-3-carboxylic acid.

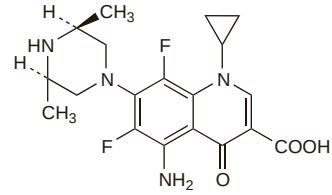
Спарфлоксацин

$C_{19}H_{22}F_2N_4O_3$ = 392.4.

CAS — 110871-86-8.

ATC — J01MA09.

ATC Vet — QJ01MA09.



Pharmacopoeias. In *Chin.*

Adverse Effects and Precautions

As for Ciprofloxacin, p.244.

Concern over phototoxicity associated with sparfloxacin has led to restriction of its use in some countries; patients should be advised to avoid exposure to sunlight during, and for a few days after, sparfloxacin therapy, and to stop the drug immediately if phototoxicity occurs.

Photosensitivity. In a survey[1] of the reporting rate for phototoxicity associated with sparfloxacin in France, the manufacturer or the French Pharmacovigilance System received 371 reports of severe phototoxic reactions during the first 9 months after marketing of the drug; this approximated to between 4 and 25 times the rate reported for other fluoroquinolones.

1. Pierfitte C, *et al.* The link between sunshine and phototoxicity of sparfloxacin. *Br J Clin Pharmacol* 2000; **49:** 609–12.

Interactions

As for Ciprofloxacin, p.246.

Sparfloxacin does not appear to interact with theophylline or caffeine, nor with warfarin or cimetidine. Probenecid does not alter the pharmacokinetics of sparfloxacin.

Antimicrobial Action

As for Ciprofloxacin, p.246.

Sparfloxacin is reported to be more active *in vitro* than ciprofloxacin against mycobacteria and against Gram-positive bacteria, including *Streptococcus pneumoniae* and other streptococci and staphylococci.

Pharmacokinetics

Sparfloxacin is well absorbed from the gastrointestinal tract with a bioavailability of about 90%. Peak plasma concentrations occur 3 to 6 hours after a dose. Sparfloxacin is widely distributed into body tissues and fluids, including respiratory tissues, but is only about 45% bound to plasma proteins. It is metabolised in the liver by glucuronidation and has an elimination half-life of about 20 hours. It is excreted in equal amounts in the faeces and urine as unchanged drug and as the glucuronide metabolite.

◊ References.

1. Shimada J, *et al.* Clinical pharmacokinetics of sparfloxacin. *Clin Pharmacokinet* 1993; **25:** 358–69.

Uses and Administration

Sparfloxacin is a fluoroquinolone antibacterial with actions and uses similar to those of ciprofloxacin (p.247). It is given orally for the treatment of susceptible infections in a usual dose of 100 to 300 mg in 1 or 2 divided doses daily. It has also been tried in tuberculosis (see under Uses and Administration of Ciprofloxacin, p.248).

◊ General references.

1. Finch RG, *et al.*, eds. Sparfloxacin: focus on clinical performance. *J Antimicrob Chemother* 1996; **37** (suppl A): 1–167.
2. Goa KL, *et al.* Sparfloxacin: a review of its antibacterial activity, pharmacokinetic properties, clinical efficacy and tolerability in lower respiratory tract infections. *Drugs* 1997; **53:** 700–25.
3. Martin SJ, *et al.* Levofloxacin and sparfloxacin: new quinolone antibiotics. *Ann Pharmacother* 1998; **32:** 320–36.
4. Schentag JJ. Sparfloxacin: a review. *Clin Ther* 2000; **22:** 372–87.

Preparations

Proprietary Preparations (details are given in Part 3)
Cz.: Zagam†; ***India:*** Scat; Sparbact; Sparcip; Spardac; Spardrops; Sparquin; Sparvista; Sparx; ***Indon.:*** Newspar; Resflok; Sparos; ***Jpn:*** Spara; ***Rus.:*** Sparflo (Спарфло); ***USA:*** Zagam†.

Spectinomycin *(BAN, rINN)*

Actinospectacin; Espectinomicina; Spectinomycine; Spectinomycinum; Spektinomycin; Spektinomysiini. Perhydro-4a,7,9-trihydroxy-2-methyl-6,8-bis(methylamino)pyrano[2,3-*b*][1,4]benzodioxin-4-one.

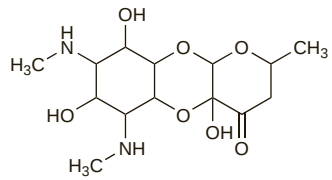
Спектиномицин

$C_{14}H_{24}N_2O_7$ = 332.3.

CAS — 1695-77-8.

ATC — J01XX04.

ATC Vet — QJ01XX04.



Description. Spectinomycin is an antimicrobial substance produced by the growth of *Streptomyces spectabilis* or by any other means.

Spectinomycin Hydrochloride *(BANM, USAN, rINNM)*

Hidrocloruro de espectinomicina; M-141; Spectinomycine, Chlorhydrate de; Spectinomycine (dichlorhydrate de) pentahydraté; Spectinomycini dihydrochloridum pentahydricum; Spectinomycini hydrochloridum; Spektinomicin-hidroklorid; Spektinomicino hidrochloridas; Spektinomycin hydrochlorid; Spektinomycindihydrokloridpentahydrat; Spektinomysiinidihydrokloridipentahydraatti; Spektynomycyny chlorowodorek; Spektynomycyny dichlorowodorek pięciowodny; U-18409AE. Spectinomycin dihydrochloride pentahydrate.

Спектиномицина Гидрохлорид

$C_{14}H_{24}N_2O_7,2HCl,5H_2O$ = 495.3.

CAS — 21736-83-4 (anhydrous spectinomycin hydrochloride); 22189-32-8 (spectinomycin hydrochloride pentahydrate).

ATC — J01XX04.

ATC Vet — QJ01XX04.

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

Ph. Eur. 6.2 (Spectinomycin Dihydrochloride Pentahydrate). A substance produced by *Streptomyces spectabilis* or by any other means. A white or almost white, slightly hygroscopic, powder. Freely soluble in water; very slightly soluble in alcohol. A 10% solution in water has a pH of 3.8 to 5.6. Store in airtight containers.

USP 31 (Spectinomycin Hydrochloride). A white to pale buff crystalline powder. 1 mg of monograph substance has a potency equivalent to not less than 603 micrograms of spectinomycin. Freely soluble in water; practically insoluble in alcohol, in chloroform, and in ether. A 1% solution in water has a pH of 3.8 to 5.6. Store in airtight containers.

Adverse Effects and Precautions

Nausea, dizziness, fever and chills, insomnia, and urticaria have occasionally occurred with single doses of spectinomycin. Anaphylaxis has occurred rarely. Mild to moderate pain has been reported after intramuscular injections. Alterations in kidney and liver function and a decrease in haemoglobin and haematocrit have occasionally been seen with repeated doses. Although a reduction in urine output has been seen after single and multiple doses, spectinomycin has not been noted to produce functional changes indicative of nephrotoxicity.

Spectinomycin is ineffective in the treatment of syphilis and patients being treated for gonorrhoea should be observed for evidence of syphilis.

Interactions

Lithium. For the effect of spectinomycin on lithium, see Antimicrobials, under Interactions of Lithium, p.404.

Antimicrobial Action

Spectinomycin is an aminocyclitol antibacterial that acts by binding to the 30S subunit of the bacterial ribosome and inhibiting protein synthesis. Its activity is generally modest, particularly against Gram-positive organisms. Anaerobic organisms are mostly resistant. Various Gram-negative organisms are sensitive, including many enterobacteria and also *Haemophilus ducreyi*, and it is particularly effective against *Neisseria gonorrhoeae*. Although generally bacteriostatic, spectinomycin is bactericidal against susceptible gonococci at concentrations not much above the MIC.

Resistance may develop by chromosomal mutation or may be plasmid-mediated in some organisms; resistant gonococci have been reported clinically, notably in the Far East, but in most parts of the world resistant neisserial strains have been uncommon to date.

Pharmacokinetics

Spectinomycin is poorly absorbed orally but is rapidly absorbed after the intramuscular injection of the hydrochloride. A 2-g dose produces peak plasma concentrations of about 100 micrograms/mL at 1 hour while a 4-g dose produces peak concentrations of about 160 micrograms/mL at 2 hours. Therapeutic plasma concentrations are maintained for up to 8 hours. Distribution into saliva is poor (which limits its value in pharyngeal gonorrhoea). It is poorly bound to plasma proteins. Spectinomycin is excreted in an active form in the urine and up to 100% of a dose has been recovered within 48 hours. A half-life of about 1 to 3 hours has been reported; it is prolonged in patients with renal impairment. Spectinomycin is partially removed by dialysis.

Uses and Administration

Spectinomycin is used as an alternative to cephalosporins or fluoroquinolones in the treatment of gonorrhoea (p.191) although poor distribution into saliva limits its usefulness in pharyngeal infections. It has also been used in the treatment of chancroid (p.191).

Spectinomycin is given as the hydrochloride but doses are expressed in terms of the base. Spectinomycin hydrochloride 1.5 g is equivalent to about 1 g of spectinomycin. In the treatment of gonorrhoea it is given by deep intramuscular injection as a single dose equivalent to 2 g of spectinomycin, although a dose of 4 g may sometimes be required, divided between two injection sites. Multiple-dose courses have been used for the treatment of disseminated infections.

Spectinomycin is not effective against syphilis or chlamydial infections and additional therapy for these infections may also be needed.

For details of doses in children, see below.

Administration in children. Parenteral spectinomycin is not recommended in neonates because of the presence of benzyl alcohol, a preservative that has been associated with fatalities in neonates due to the 'gasping syndrome' (see p.1632).

For prophylaxis in neonates born to mothers with gonorrhoea WHO recommends a single intramuscular dose of spectinomycin 25 mg/kg (maximum 75 mg) as an alternative to ceftriaxone. The CDC recommends spectinomycin as an alternative to cephalosporins in the treatment of uncomplicated gonorrhoea (p.191) in children beyond the newborn period and weighing under 45 kg; a single intramuscular dose equivalent to 40 mg/kg of spectinomycin may be given.

Preparations

USP 31: Spectinomycin for Injectable Suspension.

Proprietary Preparations (details are given in Part 3)

Arg.: Togamycin†; ***Austral.:*** Trobicin; ***Austria:*** Trobicin; ***Belg.:*** Trobicin; ***Braz.:*** Trobicin†; ***Fr.:*** Trobicine; ***Ger.:*** Stanilo; ***Hong Kong:*** Kirin; Trobicin; ***India:*** Spectin; Trobicin; ***Israel:*** Togamycin†; ***Ital.:*** Trobicin; ***Malaysia:*** Kirin†; ***Mex.:*** Trobicin; ***Port.:*** Trobicin†; ***Rus.:*** Kirin (Кирин); Trobicin (Тробицин)†; ***S.Afr.:*** Trobicin; ***Singapore:*** Trobicin; ***Spain:*** Kempi; ***Switz.:*** Trobicin; ***Thai.:*** Trobicin; Vabicin; ***Venez.:*** Trobicin†.

Spiramycin *(BAN, USAN, rINN)*

Espiramicina; IL-5902; NSC-55926; NSC-64393 (spiramycin hydrochloride); RP-5337; Spiramicin; Spiramicinas; Spiramisin; Spiramycine; Spiramycinum; Spiramysiini. A mixture comprised principally of (4*R*,5*S*,6*S*,7*R*,9*R*,10*R*,16*R*)-(11*E*,13*E*)-6-[(*O*-2,6-dideoxy-3-*C*-methyl-α-L-*ribo*-hexopyranosyl)-(1→4)-(3,6-dideoxy-3-dimethylamino-β-D-glucopyranosyl)oxy]-7-formylmethyl-4-hydroxy-5-methoxy-9,16-dimethyl-10-[(2,3,4,6-tetradeoxy-4-dimethylamino-D-*erythro*-hexopyranosyl)oxy]oxacyclohexadeca-11,13-dien-2-one (Spiramycin I).

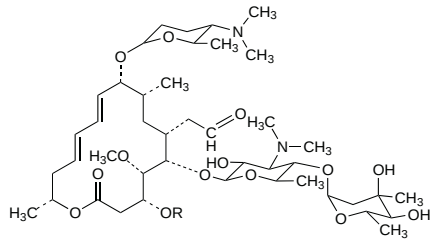
Спирамицин

$C_{43}H_{74}N_2O_{14}$ = 843.1.

CAS — 8025-81-8.

ATC — J01FA02.

ATC Vet — QJ01FA02; QJ51FA02.



Spiramycin I R = H
Spiramycin II R = $COCH_3$
Spiramycin III R = $COCH_2CH_3$

Pharmacopoeias. In *Eur.* (see p.vii). Also in *BP (Vet). Jpn* includes Acetylspiramycin.

Ph. Eur. 6.2 (Spiramycin). A macrolide antibiotic produced by the growth of certain strains of *Streptomyces ambofaciens* or obtained by any other means. The potency is not less than 4100 units/mg, calculated with reference to the dried substance. A white or slightly yellowish, slightly hygroscopic powder. Slightly soluble in water; freely soluble in alcohol, in acetone, and in methyl alcohol. A 0.5% solution in methyl alcohol and water has a pH of 8.5 to 10.5. Store in airtight containers.

Adverse Effects and Precautions

As for Erythromycin, p.270.

The most frequent adverse effects are gastrointestinal disturbances. Transient paraesthesia has been reported during parenteral use.

Interactions

For a discussion of drug interactions of macrolide antibacterials, see Erythromycin, p.271.

Cytochrome P450 isoenzymes. Spiramycin is reported to have little or no effect on hepatic cytochrome P450 isoenzymes and may therefore produce fewer interactions than erythromycin with other drugs metabolised by this enzyme system (see Mechanism, under Interactions of Erythromycin, p.271). The lack of interactions between spiramycin and theophylline and ciclosporin would appear to support this. Nevertheless, a report of torsade de pointes in a patient with a congenital long QT syndrome during treatment with spiramycin and *mequitazine*[1] suggests that caution is still needed.

Reduced plasma concentrations of *levodopa* have been reported when given with spiramycin (see p.807).

1. Verdun F, *et al.* Torsades de pointes sous traitement par spiramycine et méquitazine: à propos d'un cas. *Arch Mal Coeur Vaiss* 1997; **90:** 103–6.

Antimicrobial Action

As for Erythromycin, p.271, although it is somewhat less active *in vitro* against many species. It is active against *Toxoplasma gondii*.

Pharmacokinetics

Spiramycin is incompletely absorbed from the gastrointestinal tract and absorption is reduced by food. It is widely distributed into tissues, although it does not cross the blood-brain barrier. Spiramycin crosses the placenta and is distributed into breast milk. Plasma protein binding ranges from 10 to 25%. An oral dose of 6 million units produces peak blood concentrations of 3.3 micrograms/mL after 1.5 to 3 hours; the half-life is about 5 to 8 hours. High tissue concentrations are achieved and persist long after the plasma concentration has fallen to low levels.

Spiramycin is metabolised in the liver to active metabolites; substantial amounts are excreted in the bile and about 10% in the urine.

Uses and Administration

Spiramycin is a macrolide antibacterial that is used similarly to erythromycin (p.272) in the treatment of susceptible bacterial infections. It has also been used in the protozoal infections cryptosporidiosis (p.823) and toxoplasmosis (p.826).

Spiramycin is given orally as the base or intravenously as the adipate; it has also been given rectally as the adipate. The usual oral adult dose is 6 to 9 million units daily, in 2 or 3 divided doses. Doses of up to 15 million units have been given daily in divided doses for severe infections. A dose of 1.5 million units of spiramycin may be given by slow intravenous infusion every 8 hours; in severe infection the dose may be doubled.

Spiramycin is available in combination preparations with metronidazole in some countries.

Acetylspiramycin is also used.

◊ Reviews.

1. Rubinstein E, Keller N. Spiramycin renaissance. *J Antimicrob Chemother* 1998; **42:** 572–6.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Rovamycine; ***Austria:*** Rovamycin; ***Belg.:*** Rovamycine; ***Braz.:*** Rovamicina; ***Canad.:*** Rovamycine†; ***Cz.:*** Rovamycine; ***Fr.:*** Rovamycine; ***Ger.:*** Rovamycine; Selectomycin; ***Gr.:*** Rovamycine; ***Hong Kong:*** Rovamycine; ***Hung.:*** Rovamycine; ***India:*** Rovamycin; ***Indon.:*** Ethirov; Hypermycin; Ismacrol; Medirov; Osmycin; Provamed; Rofacin; Rovadin; Rovamycine; Sorov; Spirabiotic; Spiradan; Spiranter; Spirasin; Varoc; Vipram; ***Israel:*** Rovamycine; ***Ital.:*** Rovamicina; Spiromix; ***Malaysia:*** Rovamycine; ***Mex.:*** Provamicina; ***Neth.:*** Rovamycine; ***Norw.:*** Rovamycin; ***Pol.:*** Rovamycine; ***Port.:*** Rovamycine; ***Rus.:*** Rovamycine (Ровамицин); ***Singapore:*** Rovamycine; ***Spain:*** Dicorvin; Rovamycine; ***Switz.:*** Rovamycine; ***Thai.:*** Rovamycin; Spiracin; ***Turk.:*** Rovamycine; ***Venez.:*** Provamicina.

Multi-ingredient: ***Arg.:*** Estilomicin; ***Braz.:*** Periodontil; ***Cz.:*** Rodogyl†; ***Fr.:*** Birodogyl; Missilor; Rodogyl; ***Malaysia:*** Rodogyl; ***Mex.:*** Rodogyl; ***Spain:*** Rhodogil.

Streptomycin *(BAN, rINN)*

Estreptomicina; Streptomisin; Streptomycine; Streptomycinum; Streptomysiini. *O*-2-Deoxy-2-methylamino-α-L-glucopyranosyl-(1→2)-*O*-5-deoxy-3-*C*-formyl-α-L-lyxofuranosyl-(1→4)-*N*^{3},*N*^{3}-diamidino-D-streptamine.

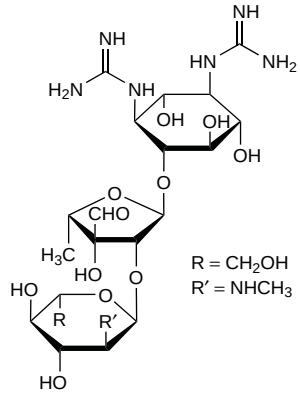
Стрептомицин

$C_{21}H_{39}N_7O_{12}$ = 581.6.

CAS — 57-92-1.

ATC — A07AA04; J01GA01.

ATC Vet — QA07AA04; QJ01GA01.



Description. An antimicrobial organic base produced by the growth of certain strains of *Streptomyces griseus*, or by any other means.

Streptomycin Hydrochloride *(BANM, rINNM)*

Hidrocloruro de estreptomicina; Streptomycine, Chlorhydrate de; Streptomycini Hydrochloridum.

Стрептомицина Гидрохлорид

$C_{21}H_{39}N_7O_{12}$,3HCl = 691.0.

CAS — 6160-32-3.

ATC — A07AA04; J01GA01.

ATC Vet — QA07AA04; QJ01GA01.

Streptomycin Sulfate *(rINNM)*

Streptomicino sulfatas; Streptomycin Sesquisulphate; Streptomycin sulfát; Streptomycin Sulphate *(BANM)*; Streptomycine, sulfate de; Streptomycini sulfas; Streptomycinsulfat; Streptomycyny siarczan; Streptomysiinisulfaatti; Sulfato de estreptomicina; Sztreptomicin-szulfát.

Стрептомицина Сульфат

$(C_{21}H_{39}N_7O_{12})_2$,$3H_2SO_4$ = 1457.4.

CAS — 3810-74-0.

ATC — A07AA04; J01GA01.

ATC Vet — QA07AA04; QJ01GA01.

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

Ph. Eur. 6.2 (Streptomycin Sulphate). A white or almost white, hygroscopic powder. The potency is not less than 720 units/mg, calculated with reference to the dried substance. Very soluble in water; practically insoluble in dehydrated alcohol. A 25% solution in water has a pH of 4.5 to 7.0. Store in airtight containers.

USP 31 (Streptomycin Sulfate). A white or practically white, hygroscopic powder; odourless or with not more than a faint odour. It has a potency equivalent to not less than 650 micrograms and not more than 850 micrograms of streptomycin per mg. Freely soluble in water; very slightly soluble in alcohol; practically insoluble in chloroform. A solution in water containing the equivalent of streptomycin 20% has a pH of 4.5 to 7.0. Store in airtight containers.

Incompatibility. Streptomycin sulfate is incompatible with acids and alkalis.

Adverse Effects, Treatment, and Precautions

As for Gentamicin Sulfate, p.282. Like gentamicin the ototoxic effects of streptomycin are mainly vestibular rather than auditory. Ototoxicity has been seen in