### 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†.

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## 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).

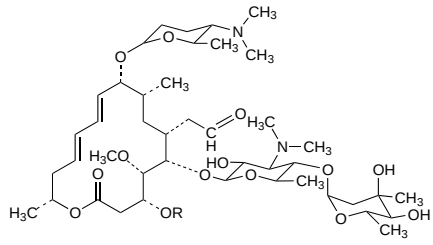
Спирамицин

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

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## 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.

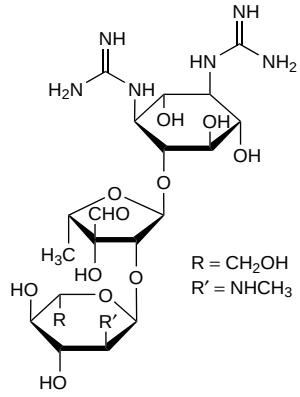
Стрептомицин

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