

About 50% of a single dose of sulfadiazine given by mouth is excreted in the urine in 24 hours; 15 to 40% is excreted as the acetyl derivative.

◇ The urinary excretion of sulfadiazine and the acetyl derivative is dependent on pH. About 30% is excreted unchanged in both fast and slow acetylators when the urine is acidic whereas about 75% is excreted unchanged by slow acetylators when the urine is alkaline. The half-life of sulfadiazine ranges from 7 to 12 hours and that of its metabolite from 8 to 12 hours.¹

1. Vree TB, et al. Determination of the acetylator phenotype and pharmacokinetics of some sulphonamides in man. *Clin Pharmacol* 1980; 5: 274-94.

Uses and Administration

Sulfadiazine is a short-acting sulfonamide that has been used similarly to sulfamethoxazole (p.341) in the treatment of infections due to susceptible organisms. It has been used in the treatment of nocardiosis and lymphogranuloma venereum, and has been given for the prophylaxis of rheumatic fever in penicillin-allergic patients. For details of these infections and their treatment, see Choice of Antibacterial, p.162. Sulfadiazine is also given with pyrimethamine for the treatment and prevention of relapse of toxoplasmosis (p.826) and has been tried in disseminated *Acanthamoeba* infection (p.822).

In the treatment of susceptible infections, sulfadiazine may be given orally in usual initial doses of 2 to 4 g, followed by up to 6 g daily in divided doses. A dose in children is 75 mg/kg initially, then 150 mg/kg daily in divided doses to a maximum of 6 g daily. Sulfadiazine is used in infants less than 2 months of age for congenital toxoplasmosis; an oral dose of 50 mg/kg twice daily for 12 months has been suggested by the *BNFC* for use in neonates.

Immunocompromised patients who have toxoplasmosis should be given a dose of 4 to 6 g daily in 4 divided doses for at least 6 weeks, followed by a suppressive dose of 2 to 4 g daily, which should continue indefinitely. Pyrimethamine should always be given as well.

For the prophylaxis of rheumatic fever, patients weighing less than about 30 kg are given 500 mg once daily, while those over 30 kg may receive 1 g once daily.

Sulfadiazine is also given intravenously as the sodium salt. Sulfadiazine sodium 1.09 g is equivalent to about 1 g of sulfadiazine. The usual dose is the equivalent of sulfadiazine 2 to 3 g initially, then 1 g four times daily for 2 days; subsequent treatment is given orally. Children and infants over 2 months of age may be given the equivalent of 50 mg/kg initially, followed by 25 mg/kg four times daily.

Intravenous doses of sulfadiazine sodium are given by infusion or by slow intravenous injection of a solution containing up to 5% sulfadiazine. It may be diluted with sodium chloride 0.9%. Sulfadiazine sodium has been given by deep intramuscular injection, but great care must be taken to prevent damage to subcutaneous tissues; the intravenous route is preferred.

Sulfadiazine has been used with trimethoprim as cotrimazine (p.258). Sulfadiazine has also been used with other sulfonamides, particularly sulfamerazine and sulfadimidine, to reduce the problems of low solubility in urine.

Preparations

BP 2008: Sulfadiazine Injection;

USP 31: Sulfadiazine Sodium Injection; Sulfadiazine Tablets; Trisulfapyrimidines Oral Suspension; Trisulfapyrimidines Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Sulfatril; **Braz.:** Neo Sulfazina†; Suladrin; Sulfadiazinac†; **Fr.:** Adiazine†; **Gr.:** Adiazine; **Mex.:** Bioarginol-C; Sularyn; **Port.:** Labdiazina.

Multi-ingredient: **Arg.:** Afonisan; Anginotrat; Pastillas Lorbi; Sulfatral-Ce-no†; **Austria:** Ophcllin N; Rhinon; **Braz.:** Triglobe; **Canad.:** Coptin; **Fin.:** Ditrin; Trimetin Duplo; **Ger.:** Sterinor†; Urospasmon sine†; Urospasmon†; **Gr.:** Geypinna; **India:** Aubnil; Zad-G; **Indon.:** Trisulfa; **Malaysia:** Balin; Beaglobe; Triglobe†; Trisulprim†; Trizine; **Mex.:** Agin; Estrefren; **Philipp.:** Triglobe; Trizine; **Port.:** Broncodiazina; **Singapore:** Balin; **Swed.:** Trimin sulfat†; **Thai.:** Sulfatril; **Turk.:** Sulfatrim; **Venez.:** Esterinor†.

Sulfadiazine Silver (BANM, rINNM)

Argenti Sulfadiazinum; Gümüş Sulfadiazin; Hopeasulfadiatsiini; Silver Sulfadiazine (USAN); Silver Sulphadiazine; Silversulfadiazin; Sulfadiazina argéntica; Sulfadiazine Argentique; Sulfadiazinum Argentum; Sulfadiazinum Argentum; Sulphadiazine Silver.

Сульфадиазин Серебра

$C_{10}H_9AgN_4O_2S = 357.1$.

CAS — 22199-08-2.

ATC — D06BA01.

ATC Vet — QD06BA01.

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

USP 31 (Silver Sulfadiazine). A white to creamy-white, odourless or almost odourless crystalline powder. It becomes yellow on exposure to light. Practically insoluble in alcohol, in chloroform, and in ether; slightly soluble in acetone; freely soluble in 30% ammonia solution. It decomposes in moderately strong mineral acids. Protect from light.

Adverse Effects, Treatment, and Precautions

Sulfadiazine silver may be absorbed after topical application and produce systemic effects similar to those of other sulfonamides (see Sulfamethoxazole, p.340).

Local pain or irritation are uncommon; the separation of the eschar may be delayed and fungal invasion of the wound may occur.

Transient leucopenia does not usually require withdrawal of sulfadiazine silver, but blood counts should be monitored to ensure they return to normal within a few days. Systemic absorption of silver, resulting in argyria, can occur when sulfadiazine silver is applied to large area wounds or over prolonged periods.

Argyria. A report of argyria, with discoloration of the skin and sensorimotor neuropathy, caused by excessive application of sulfadiazine silver 1% cream to extensive leg ulcers.¹

1. Payne CMER, et al. Argyria from excessive use of topical silver sulphadiazine. *Lancet* 1992; 340: 126.

Effects on the kidneys. For mention of renal failure and leucopenia associated with the use of sulfadiazine silver see under Sulfadiazine, above.

Interactions

As for Sulfamethoxazole, p.341.

Sulfadiazine silver is not antagonised by *p*-aminobenzoic acid or related compounds. The silver content of sulfadiazine silver may inactivate enzymatic debriding agents.

Antimicrobial Action

Sulfadiazine silver has broad antimicrobial activity against Gram-positive and Gram-negative bacteria including *Pseudomonas aeruginosa*, and some yeasts and fungi. Sulfadiazine silver has a bactericidal action; in contrast to sulfadiazine, the silver salt acts primarily on the cell membrane and cell wall and its action is not antagonised by *p*-aminobenzoic acid. Resistance to sulfadiazine silver has been reported and may develop during therapy.

Pharmacokinetics

Sulfadiazine silver slowly releases sulfadiazine when in contact with wound exudates. Up to about 10% of the sulfadiazine may be absorbed; concentrations in blood of 10 to 20 micrograms/mL have been reported, although higher concentrations may be achieved when extensive areas of the body are treated. Some silver may also be absorbed.

Uses and Administration

Sulfadiazine silver is a sulfonamide that is used, in conjunction with debridement, as a 1% cream for the prevention and treatment of infection in severe burns (p.1578).

Sulfadiazine silver has also been used in other skin conditions, such as leg ulcers (p.1585), where infection may prevent healing and for the prophylaxis of infec-

tion in skin grafting. It has also been applied to the eyes in the treatment of superficial *Aspergillus* infections.

Catheters impregnated with sulfadiazine silver have been used to reduce catheter colonisation and related bloodstream infection (p.1624).

Preparations

USP 31: Silver Sulfadiazine Cream.

Proprietary Preparations (details are given in Part 3)

Arg.: Silverderma†; **Austria:** Flammazine; **Belg.:** Flammazine; Sulfasil; **Braz.:** Dermazine; Gino Dermazine; Pratazine†; Silgos; Sulfaderm; **Canad.:** Dermazine†; Flammazine; SSD†; **Cz.:** Dermazin; Flammazine†; **Denm.:** Flammazine; **Fin.:** Flammazine; **Fr.:** Flammazine; Sicazine; **Ger.:** Brandiazin; Flammazine; Urgotul S.Ag; **Gr.:** Flammazine; **Hong Kong:** Aldo-Silverderma; Dermazin; Flammazine; **Hung.:** Dermazin; **India:** SSZ; **Indon.:** Burnazin; **Irl.:** Flammazine; **Israel:** Silverol; **Ital.:** Bactermil; Sofargen; **Mex.:** Argemol; Argentaflil; Argental; Silvadene; Zitep; **Neth.:** Flammazine; **Norw.:** Flammazine; Flammazine; Innoxiderm; Sterizol; **Pol.:** Dermazin; **Port.:** Flammazine; Sicazine; Silverderma; Silvespray; **Rus.:** Dermazin (Дермажин); Silverderma (Сильведерм); Sulphargin (Сульфаргин); **S.Afr.:** Argent-Eze; Bactrazine; Flammazine; Silbecor; **Singapore:** Flammazine†; **Spain:** Flammazine; Silverderma; **Switz.:** Flammazine; Silvertone; **Thai.:** Dermazin; Flammazine; Silverol†; **Turk.:** Silvadene; Silvadiazin; Silvadene; Silverdin; **UAE:** Silvadiazin; **UK:** Flammazine; **USA:** Silvadene; SSD; Thermozone; **Venez.:** Menaderm; Protosulfil; Silverderma.

Multi-ingredient: **Arg.:** Iurónico Biotic; Platsul A; Sulfadiazina de Plata; Sulfaplat; **Austral.:** Silvazine; **Belg.:** Flammacerium; **Braz.:** Dermacerium; **Canad.:** Flammazine C†; **Chile:** KCE; Hebermin†; Platsul A; **Cz.:** Flammacerium†; Ialugen Plus; **Fr.:** Altreet Ag; Flammacerium; Ialuset Plus; Urgotul S.Ag; **Gr.:** Flammacerium; **Hung.:** Ialugen Plus; **India:** Argsept†; Burnheal†; Silverex; **Ital.:** Altergen; Connetivina Plus; **Neth.:** Flammacerium; **NZ:** Silvazine; **Philipp.:** Flammacerium; **Pol.:** Flammacerium; **Singapore:** Silvazine; Silvin; **Spain:** Unital Complex†; **Switz.:** Ialugen Plus; **UK:** Flammacerium; Physiotulle-Ag.

Sulfadiazine Silver (BANM, rINNM)

Sulfadiazine Silver; Sulfadiazine Silver; Sulfadiazine Silver; Sulfadiazine Silver.

$C_{10}H_9AgN_4O_2S = 357.1$.

CAS — 22199-08-2.

ATC — D06BA01.

ATC Vet — QD06BA01.

ATC — S01AB03.

ATC Vet — Q501AB03.

Profile

Sulfadiazine silver is a sulfonamide with properties similar to those of sulfamethoxazole (p.340). It is applied as a 15% ointment for superficial infections of the eye.

Preparations

Proprietary Preparations (details are given in Part 3)

Denm.: Irgamid†; **Fin.:** Irgamid†; **Hung.:** Irgamid†; **Switz.:** Irgamid.

Sulfadimethoxine (BAN, rINN)

Solfadimetossina; Solfadimetossipirimidina; Sulfadiméthoxine; Sulfadimethoxinum; Sulfadimetoksiini; Sulfadimethoxin; Sulfadimethoxina; Sulphadimethoxine. *N*-(2,6-Dimethoxy-pyrimidin-4-yl)-sulphanilamide.

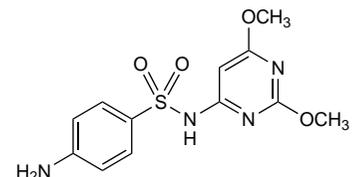
Сульфадиметоксин

$C_{12}H_{14}N_4O_4S = 310.3$.

CAS — 122-11-2.

ATC — J01ED01.

ATC Vet — QJ01EQ09; QP51AG02.



Pharmacopoeias. In *Fr.* and *It.* In *US* for veterinary use only.

USP 31 (Sulfadimethoxine). Practically white, crystalline powder. Practically insoluble in water; slightly soluble in alcohol, in chloroform, in ether, and in hexane; soluble in 2N sodium hydroxide; sparingly soluble in 2N hydrochloric acid. Store in airtight containers. Protect from light.

Profile

Sulfadimethoxine is a long-acting sulfonamide with properties similar to those of sulfamethoxazole (p.340). It is used in preparations for the treatment of skin infections and was formerly used for the treatment of urinary-tract infections. It is also used in veterinary medicine, sometimes with baquiloprim or ormetoprim.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: **Rus.:** Levosin (Левосин).