

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 Pharmacokinet* 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 cotrimoxazole (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.: Sulfaftal; Braz.: Neo Sulfazina†; Suladrin; Sulfadiazinac†; Fr.: Adiazine†; Gr.: Adiazine; Mex.: Biarginol-C; Sularyn; Port.: Labdiazina.

Multi-ingredient: Arg.: Afonsan; Anginotrat; Pastillas Lorbi; Sulfaftal-Ceno†; Austria: Opchillin N; Rhinor; Braz.: Triglobe; Canad.: Captin; Fin.: Ditrin; Trimeten Duplo; Ger.: Sterinol†; Urospasmon sinet†; Urospasmont†; Gr.: Geypirina; India: Aubril; Zad-G; Indon.: Trisula; Malaysia: Balin; Beaglebor; Triglobe; Trisulprim†; Trizine; Mex.: Agin; Estrefen; Philipp.: Triglobe; Trizine; Port.: Broncodiazina; Singapore: Balin; Swed.: Trimin sulfat†; Thai.: Sulfatrin; Turk.: Sulfatrin; Venez.: Esterinol†.

Sulfadiazine Silver (BANM, rINN)

Argenti Sulfadiazinum; Gümüş Sulfadiazin; Hopeasulfadiatsiini; Silver Sulfadiazine (USAN); Silver Sulphadiazine; Silversulfadiazin; Sulfadiazina argéntica; Sulfadiazine Argentique; Sulfadiazinum Argenticum; 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 discolouration 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.: Dermazina; Gino Dermazina; Pratazine†; Siglos; Sulfaderm; Canad.: Dermazin†; Flammaze; Fr.: Flammazine; Sicazine; Denm.: Flammaze; Fin.: Flammaze; Fr.: Flammazine; Sicazine; Ger.: Brandiazin; Flammaze; Ur-gotul SA; Gr.: Flammaze; Hong Kong: Aldo-Silverderma; Dermazin; Flammaze; Hung.: Dermazin; India: SSZ; Indon.: Burnazin; Irl.: Flammaze; Israel: Silverol†; Ital.: Bacternil; Sofargen; Mex.: Argemol; Argentafil; Argental; Silvadene; Zitep; Neth.: Flammaze; Norw.: Flammaze; Philipp.: Flammaze; Innoxiderm; Sterzol; Pol.: Dermazin; Port.: Flammaceum; Silvederma (Сильдерма); Silvespray; Rus.: Dermazin (Дермажин); Silvederma (Сильдерма); Sulphargin (Сульфаргин); SAfr.: Argent-Eze; Bactramine; Flammaze; Silbecor; Singapore: Flammaze; Spain: Flammaze; Silvederma; Switz.: Flammaze; Silvertone; Thai.: Dermazin; Flammaze; Silverol†; Turk.: Silvadene; Silvadzin; Silvamed; Silverpond; UAE: Silvadiazin; UK: Flammaze; USA: Silvadene; SSD: Thermazene; Venez.: Menaderm; Protosulf; Silvederma.

Multi-ingredient: Arg.: Iuronico Biotic; Platsul A; Sulfadiazina de Plata; Sulfaplat; Austral.: Silvazine; Belg.: Flammacerium; Braz.: Dermacerium; Canad.: Flammazine C†; Chile: FCE; Hebermin†; Platsul A; Cz.: Flammacerium†; Ialugen Plus; Fr.: Altreet Ag; Flammacerium; Ialuset Plus; Urgotul 5Ag; Gr.: Flammacerium; Hung.: Ialugen Plus; India: Argisept; Burnheal; Silverex; Ital.: Altergen Connettivina Plus; Neth.: Flammacerium; NZ: Silvazine; Philipp.: Flammacerium; Pol.: Flammacerium; Singapore: Silvazine; Silvin; Spain: Unital Complex†; Switz.: Ialugen Plus; UK: Flammacerium; Physiotulle-Ag.

Sulfadicramide (rINN)

Sulfadicramida; Sulfadicramidum; Sulfadikramid; Sulfadikramidi. N-(3-Dimethylacryloyl)sulphanilamide.

Сульфадикрамид

$C_{11}H_{14}N_2O_5S = 254.3$.

CAS — 115-68-4.

ATC — S01AB03.

ATC Vet — Q501AB03.

Profile

Sulfadicramide 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; Solfadimetosipirimidina; Sulfadiméthoxine; Sulfadimethoxinum; Sulfadimetoksini; Sulfadimetoxin; Sulfadimétoxina; Sulphadimethoxine. N-(2,6-Dimethoxyypyrimidin-4-yl)-sulphanilamide.

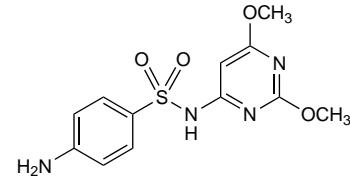
Сульфадиметоксин

$C_{12}H_{14}N_4O_5S = 310.3$.

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 air-tight 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).

Sulfadimidine (BAN, rINN)

Solfametazina; Sulfadimerazine; Sulfadimezinum; Sulfadimidiin; Sulfadimidiin; Sulfadimidina; Sulfadimidinas; Sulfadimidinum; Sulfa-methazine; Sulphadimethylpyrimidine; Sulphadimidine; Sulphamethazine; Szulfadimidin, N¹-(4,6-Dimethylpyrimidin-2-yl)sulphanilamide.

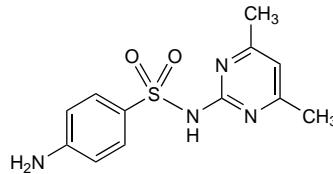
Сульфадимидин

$C_{12}H_{14}N_4O_4S = 278.3$.

CAS — 57-68-1.

ATC — J01EB03.

ATC Vet — QJ01EQ03; QP51AG01.



NOTE. Sulfadimethylpyrimidine has been used as a synonym for sulfisomidine (p.344). Care should be taken to avoid confusion between the two compounds, which are isomeric.

Pharmacopoeias. In Eur. (see p.vii), Int., US, and Viet. Also in BP (Vet).

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

USP 31 (Sulfamethazine). White to yellowish-white, practically odourless, powder. It may darken on exposure to light. Very slightly soluble in water and in ether; slightly soluble in alcohol; soluble in acetone. Protect from light.

Sulfadimidine Sodium (BANM, rINNM)

Natrii Sulfadimidinum; Soluble Sulphadimidine; Sulfadimidina sodica; Sulfadimidine Sodium; Sulfamethazine Sodium; Sulphadimidine Sodium.

Натрий Сульфадимидин

$C_{12}H_{13}N_4NaO_4S = 300.3$.

CAS — 1981-58-4.

ATC — J01EB03.

Pharmacopoeias. In Int.

Profile

Sulfadimidine is a short-acting sulfonamide with properties similar to those of sulfamethoxazole (p.340).

It is well absorbed from the gastrointestinal tract and is about 80 to 90% bound to plasma proteins. Reported half-lives have ranged from 1.5 to 4 hours in fast and 5.5 to 8.8 hours in slow acetylators. Because of the relatively high solubility of the drug and its acetyl metabolite, crystalluria may be less likely than with sulfamethoxazole.

In the treatment of susceptible infections, sulfadimidine has been given orally in an initial dose of 2 g, followed by 0.5 to 1.0 g every 6 to 8 hours. It has also been given parenterally as the sodium salt.

Sulfadimidine has also been used with other sulfonamides, particularly sulamerazine and sulfadiazine. It is also used in veterinary medicine, sometimes with baquiprim or trimethoprim.

Because its pharmacokinetics differ in fast and slow acetylators, sulfadimidine has been used to determine acetylator status.

Preparations

USP 31: Trisulfapyrimidines Oral Suspension; Trisulfapyrimidines Tablets.

Proprietary Preparations (details are given in Part 3)

Hung.: Septosyl.

Multi-ingredient: **Hung.:** Potezept; **Indon.:** Trisufa; **Thai.:** Sulfatril.

Sulfadoxine (BAN, USAN, rINN)

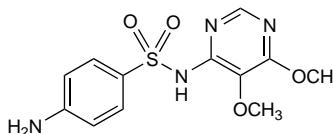
Ro-4-4393; Sulfadoksiini; Sulfadoksina; Sulfadoxin; Sulfadoxina; Sulfadoxinum; Sulformethoxine; Sulforthomidine; Sulphormethoxine; Sulphorthodimethoxine; Szulfadoxin, N¹-(5,6-Dimethoxyuridin-4-yl)sulphanilamide.

Сульфадоксин

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

CAS — 2447-57-6.

ATC Vet — QJ01EQ13.



Pharmacopoeias. In Chin., Eur. (see p.vii), Int., US, and Viet. **Ph. Eur. 6.2** (Sulfadoxine). White or yellowish-white crystalline powder or crystals. Very slightly soluble in water; slightly soluble in alcohol and in methyl alcohol. It dissolves in solutions of alkali hydroxides and in dilute mineral acids. Protect from light. **USP 31** (Sulfadoxine). Protect from light.

Adverse Effects, Treatment, and Precautions

As for Sulfamethoxazole, p.340. For reference to the adverse effects of a combination of sulfadoxine and pyrimethamine, see Pyrimethamine, p.610.

If adverse effects occur, sulfadoxine has the disadvantage that several days are required for elimination from the body.

Interactions

As for Sulfamethoxazole, p.341.

Antimicrobial Action

As for Sulfamethoxazole, p.341. Synergy exists between sulfadoxine and pyrimethamine, which act against folate metabolism at different points of the metabolic cycle.

Resistance to the combination of sulfadoxine and pyrimethamine in plasmodia, first noted in Thailand in the late 1970s, has become widespread in many malarious areas of the world. For further details of resistance to antimalarial drugs, see p.594.

Pharmacokinetics

Sulfadoxine is readily absorbed from the gastrointestinal tract. High concentrations in the blood are reached in about 4 hours; the half-life in the blood is about 4 to 9 days. About 90 to 95% is reported to be bound to plasma proteins.

Sulfadoxine is widely distributed to body tissues and fluids; it passes into the fetal circulation and has been detected in low concentrations in breast milk. Sulfadoxine is excreted very slowly in urine, primarily unchanged.

Uses and Administration

Sulfadoxine is a long-acting sulfonamide that has been used in the treatment of various infections but is now rarely used alone.

It is given as a fixed-dose combination of 20 parts sulfadoxine with 1 part pyrimethamine (*Fansidar, Roche*) in the treatment of falciparum malaria resistant to other therapies (p.594), usually after a course of quinine. Although the combination has been used in the prophylaxis of malaria, the risk of toxicity is now generally considered to outweigh its value.

In the treatment of malaria, the usual oral dose is 1.5 g of sulfadoxine with 75 mg of pyrimethamine as a single dose; this should not be repeated for at least 7 days. Oral doses for children are: 5 to 10 kg body-weight, 250 mg sulfadoxine with 12.5 mg pyrimethamine; 11 to 20 kg, 500 mg sulfadoxine with 25 mg pyrimethamine; 21 to 30 kg, 750 mg sulfadoxine with 37.5 mg pyrimethamine; 31 to 45 kg, 1 g sulfadoxine with 50 mg pyrimethamine.

Sulfadoxine with pyrimethamine has also been given intramuscularly.

Sulfadoxine with pyrimethamine has also been tried in the treatment of actinomycetomas (see Mycetoma p.180), and for prophylaxis of pneumocystis pneumonia in immunocompromised patients (see p.521 for the more usual prophylactic regimens).

A mixture of 5 parts of sulfadoxine with 1 part trimethoprim is used in veterinary medicine.

Preparations

USP 31: Sulfadoxine and Pyrimethamine Tablets.

Proprietary Preparations (details are given in Part 3)

Malaysia: Fansidar.

Multi-ingredient: **Austral.:** Fansidar; **Belg.:** Malastop; **Braz.:** Fansidar; **Canad.:** Fansidar; **Denm.:** Fansidar; **Fr.:** Fansidar; **India:** Artemal; Laridox; Pyralfin; Rimodar; **Indon.:** Fansidar; Sudcox; **Irl.:** Fansidar; **Israel:** Fansidar; **Malaysia:** Madomine; **Philipp.:** Fansidar; **S.Afr.:** Fansidar; **Singapore:** Madomine; **Switz.:** Fansidar; Fansineff; **Thail.:** Vivaxine; **UK:** Fansidar; **USA:** Fansidar.

Sulfafurazole (BAN, pINN)

Sulfafuratsoli; Sulfafurazol; Sulfafurazolas; Sulfafurazolum; Sulfisoxazole; Sulfizoksazol; Sulphafuraz; Sulphafurazole; Szulfafurazol, N¹-(3,4-Dimethylisoxazol-5-yl)sulphanilamide.

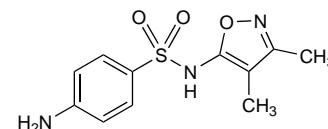
Сульфадиуразол

$C_{11}H_{13}N_3O_3S = 267.3$.

CAS — 127-69-5.

ATC — J01EB05; S01AB02.

ATC Vet — QJ01EQ05; QS01AB02.



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

Ph. Eur. 6.2 (Sulfafurazole). White or yellowish-white, crystalline powder or crystals. Practically insoluble in water; sparingly soluble in alcohol; slightly soluble in dichloromethane. It dissolves in solutions of alkali hydroxides and in dilute mineral acids. Protect from light.

USP 31 (Sulfisoxazole). A white to slightly yellowish, odourless crystalline powder. Soluble 1 in 7700 of water and 1 in 10 of boiling alcohol; soluble in 3N hydrochloric acid. Store in airtight containers. Protect from light.

Acetyl Sulfafurazole

Acetilsulfafurazol; Acetyl Sulphafurazole; Sulfisoxazole Acetyl. N¹-Acetyl Sulphafurazole; N-(3,4-Dimethylisoxazol-5-yl)-N-sulphanilylacetamide.

$C_{13}H_{15}N_3O_2S = 309.3$.

CAS — 80-74-0.

ATC — J01EB05; S01AB02.

ATC Vet — QS01AB02.

NOTE. Acetyl sulfafurazole is to be distinguished from the N⁴-acetyl derivative formed from sulfafurazole by conjugation in the body.

Compounded preparations of acetyl sulfafurazole may be represented by the following name:

- Co-erynsulfisox (PEN)—acetyl sulfafurazole and erythromycin ethyl succinate.

Pharmacopoeias. In US.

USP 31 (Sulfisoxazole Acetyl). A white or slightly yellow crystalline powder. Practically insoluble in water; soluble 1 in 176 of alcohol, 1 in 35 of chloroform, 1 in 1064 of ether, and 1 in 203 of methyl alcohol. Store in airtight containers. Protect from light.

Sulfafurazole Diolamine (pINNM)

NU-445; Sulfafurazol diolamina; Sulfafurazol, Diolamine de; Sulfafurazoli Diolaminum; Sulfisoksazol Dietanolamin; Sulfisoxazole Diolamine (USAN); Sulphafurazole Diethanolamine; Sulphafurazole Diolamine. The 2,2'-iminobisethanol salt of sulphafurazole.

Сульфадиуразол Диоламин

$C_{11}H_{13}N_3O_3S.C_4H_8NO_2 = 372.4$.

CAS — 4299-60-9.

ATC — J01EB05; S01AB02.

ATC Vet — QS01AB02.

Adverse Effects, Treatment, and Precautions

As for Sulfamethoxazole, p.340.

Sulfafurazole and its acetyl derivative are relatively soluble in urine and the risk of crystalluria is generally slight, but nevertheless adequate fluid intake is recommended.

Breast feeding. A study¹ in 6 women who received sulfafurazole concluded that the amount of drug secreted into breast milk poses no risk to the healthy infant beyond the immediate newborn period, but potential risk in breast-fed infants with jaundice or G6PD deficiency, or who are ill, stressed, or premature, was more difficult to evaluate. Based on this evidence, the American Academy of Pediatrics² has stated that sulfafurazole is usually