Interactions
As for Sulfamethoxazole, p.341.

Antimicrobial Action
As for Sulfamethoxazole, p.341.

Pharmacokinetics
Sulfamethizole is readily absorbed from the gastrointestinal tract; about 90% has been reported to be bound to plasma proteins. Its half-life has been reported to range from about 1.5 to 3 hours. It is only slightly acetylated in the body and is rapidly excreted, about 60% of a dose being eliminated in the urine in 5 hours and around 90% within 10 hours. Sulfamethizole and its acetyl derivative are readily soluble in urine over a wide pH range. Only low concentrations are achieved in blood and tissues because of its rapid excretion.

Uses and Administration
Sulfamethizole is a short-acting sulfonamide that is given orally in the treatment of infections of the urinary tract, sometimes with other antibacterials; it is unsuitable for the treatment of systemic infection since only relatively low concentrations of drug are achieved in the blood and tissues.

It is given in adult doses of 1.5 to 4 g daily in 3 or 4 divided doses. A usual dose for children is 30 to 45 mg/kg daily in 4 divided doses.

Sulfamethizole monoethanolamine has also been used.

Preparations
USP 31: Sulfamethizole Oral Suspension; Sulfamethizole Tablets.

Proprietary Preparations (details are given in Part 3)
Denm.: Lucosil; ***Fr.:*** Rufol; ***Norw.:*** Lucosil†; ***Thai.:*** Luco-Oph†.

Multi-ingredient: ***Spain:*** Micturol Sedante; ***USA:*** Urobiotic-250; ***Venez.:*** Bacteval.

Sulfamethoxazole *(BAN, USAN, rINN)*

Ro-4-2130; Sulfamethoxazol; Sulfaméthoxazole; Sulfamethoxazolum; Sulfametoksatsoli; Sulfametoksazol; Sulfametoksazolas; Sulfametoxazol; Sulfisomezole; Sulphamethoxazole; Szulfametoxazol. N^1-(5-Methylisoxazol-3-yl)sulphanilamide.

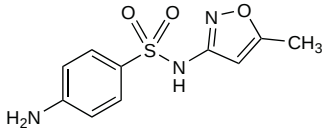
Сульфаметоксазол

$C_{10}H_{11}N_3O_3S$ = 253.3.

CAS — 723-46-6.

ATC — J01EC01.

ATC Vet — QJ01EQ11.



NOTE. Compounded preparations of sulfamethoxazole may be represented by the following names:

- Co-trimoxazole (*BAN*)—sulfamethoxazole 5 parts and trimethoprim 1 part (see p.258)
- Co-trimoxazole (*PEN*)—sulfamethoxazole and trimethoprim.

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

Ph. Eur. 6.2 (Sulfamethoxazole). A white or almost white, crystalline powder. Practically insoluble in water; sparingly soluble in alcohol; freely soluble in acetone. It dissolves in dilute solutions of sodium hydroxide and in dilute acids. Protect from light.

USP 31 (Sulfamethoxazole). A white to off-white, practically odourless, crystalline powder. Soluble 1 in 3400 of water, 1 in 50 of alcohol, and 1 in 1000 of chloroform and of ether; slowly and usually incompletely soluble 1 in 2 of carbon disulfide; freely soluble in acetone and in dilute solutions of sodium hydroxide. Protect from light.

Adverse Effects and Treatment
Nausea, vomiting, anorexia, and diarrhoea are relatively common after use of sulfamethoxazole and other sulfonamides.

Hypersensitivity reactions to sulfonamides have proved a problem. Fever is relatively common, and reactions involving the skin may include rashes, pruritus, photosensitivity reactions, exfoliative dermatitis, and erythema nodosum. Severe, potentially fatal, skin reactions including toxic epidermal necrolysis and the Stevens-Johnson syndrome have occurred in patients treated with sulfonamides. Dermatitis may also occur from contact of sulfonamides with the skin. SLE, particularly exacerbation of pre-existing disease, has also been reported.

Nephrotoxic reactions including interstitial nephritis and tubular necrosis, which may result in renal failure, have been attributed to hypersensitivity to sulfamethoxazole. Lumbar pain, haematuria, oliguria, and anuria may also occur due to crystallisation in the urine of sulfamethoxazole or its less soluble acetylated metabolite. The risk of crystalluria can be reduced by giving fluids to maintain a high urine output. If necessary, alkalinisation of the urine with sodium bicarbonate may increase solubility and aid the elimination of sulfonamides.

Blood disorders have occasionally occurred during treatment with the sulfonamides including sulfamethoxazole, and include agranulocytosis, aplastic anaemia, thrombocytopenia, leucopenia, hypoprothrombinaemia, and eosinophilia. Many of these effects on the blood may result from hypersensitivity reactions. Sulfonamides may rarely cause cyanosis due to methaemoglobinaemia. Acute haemolytic anaemia is a rare complication which may be associated with G6PD deficiency.

Other adverse effects that may be manifestations of a generalised hypersensitivity reaction to sulfonamides include a syndrome resembling serum sickness, hepatic necrosis, hepatomegaly and jaundice, myocarditis, pulmonary eosinophilia and fibrosing alveolitis, and vasculitis including polyarteritis nodosa. Anaphylaxis has been reported only very rarely.

Other adverse reactions reported after sulfamethoxazole or other sulfonamides include hypoglycaemia, hypothyroidism, neurological reactions including aseptic meningitis, ataxia, benign intracranial hypertension, convulsions, dizziness, drowsiness, fatigue, headache, insomnia, mental depression, peripheral or optic neuropathies, psychoses, tinnitus, vertigo, and pancreatitis.

Sulfonamides may displace serum-bound bilirubin, resulting in kernicterus in premature neonates.

As with other antimicrobials, sulfamethoxazole may cause alterations of the bacterial flora in the gastrointestinal tract. There is, therefore, the possibility, although it appears to be small, that pseudomembranous colitis may occur.

Slow acetylators of sulfamethoxazole may be at greater risk of adverse reactions than fast acetylators.

For further information on the adverse effects of sulfamethoxazole when used with trimethoprim, see Co-trimoxazole, p.258.

Precautions
In patients given sulfamethoxazole, adequate fluid intake is necessary to reduce the risk of crystalluria; the daily urine output should be 1200 mL or more. Compounds that render the urine acidic may increase the risk of crystalluria; the risk may be reduced with alkaline urine.

Treatment with sulfonamides should be stopped immediately a rash appears because of the danger of severe allergic reactions such as the Stevens-Johnson syndrome.

Sulfamethoxazole should be given with care to patients with renal or hepatic impairment and is contra-indicated in patients with severe impairment or with blood disorders. Dosage reduction may be necessary in renal impairment. Complete blood counts and urinalyses with microscopic examination should be carried out particularly during prolonged therapy. Sulfamethoxazole should not be given to patients with a history of hypersensitivity to sulfonamides as cross-sensitivity may occur between drugs of this group. Care is generally advisable in patients with a history of allergy or asthma. Caution is also needed in the elderly, who may be more likely to have other risk factors for reactions. Some consider sulfamethoxazole to be contra-indicated in lupus erythematosus as it may exacerbate the condition. Patients with glucose 6-phosphate dehydrogenase deficiency may be at risk of haemolytic reactions.

Sulfamethoxazole and other sulfonamides are not usually given to infants within 1 to 2 months of birth because of the risk of producing kernicterus; for the same reason, they are generally contra-indicated in women prior to delivery (see below).

Patients with AIDS may be particularly prone to adverse reactions, especially when sulfamethoxazole is given with trimethoprim as co-trimoxazole.

Sulfonamides have been reported to interfere with some diagnostic tests, including those for urea, creatinine, and urinary glucose and urobilinogen.

Breast feeding. Sulfonamides are excreted into breast milk in low concentrations and, although they are generally contra-indicated in the USA in breast-feeding women because of the risk of kernicterus, they are usually thought to pose a negligible risk to healthy neonates. However, sulfonamides should be used with caution in breast-feeding mothers of ill, stressed, or premature infants and of infants with jaundice, hyperbilirubinaemia or G6PD deficiency.

The American Academy of Pediatrics considers sulfamethoxazole, when given with trimethoprim, to be compatible with breast feeding.[1]

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)

Immunocompromised patients. Sulfamethoxazole is mainly conjugated in the liver to the N^4-acetyl derivative, but is also oxidised, to a limited extent, to the hydroxylamine metabolite.[1-5] Although this metabolite was originally implicated[6] in the development of adverse reactions to sulfonamides, recent work[7] has cast some doubt on this hypothesis. The metabolite appears to be produced through cytochrome P450 oxidative metabolism, and it has been suggested that slow acetylators of sulfamethoxazole exhibit increased oxidation compared with other metabolic routes.[1] AIDS patients also exhibit increased oxidation, since they may be depleted of substrates such as acetylcoenzyme A or glutathione necessary for acetylation or detoxification, and this may explain their susceptibility to sulfamethoxazole toxicity.[2,3]

There have been attempts to inhibit the formation of the hydroxylamine metabolite by competitive inhibition of cytochrome P450 enzymes, notably with fluconazole and ketoconazole.[4,5] Encouraging results have been obtained with fluconazole in healthy subjects, but the potential for clinical benefit in AIDS patients requires further study.[5]

However, one successful method of overcoming adverse effects in AIDS patients has been **desensitisation**. Desensitisation by use of initial doses of 4 mg of sulfamethoxazole or 5 mg of sulfadiazine every 6 hours, doubled at 24-hour intervals until the desired dose was reached, was uneventful in 9 of 13 patients with AIDS requiring sulfonamide treatment for opportunistic infections.[8] The remaining 4 had cutaneous reactions with fever, but in 2 of these the reactions were successfully managed with an antihistamine. Although there is a risk of anaphylaxis, patients with AIDS can be successfully treated with sulfonamides after desensitisation.

See also Immunocompromised Patients under Precautions of Co-trimoxazole, p.258.

1. Cribb AE, Spielberg SP. Sulfamethoxazole is metabolized to the hydroxylamine in humans. *Clin Pharmacol Ther* 1992; **51:** 522–6.
2. Lee BL, *et al.* The hydroxylamine of sulfamethoxazole and adverse reactions in patients with acquired immunodeficiency syndrome. *Clin Pharmacol Ther* 1994; **56:** 184–9.
3. van der Ven AJA, *et al.* Urinary recovery and kinetics of sulphamethoxazole and its metabolites in HIV-seropositive patients and healthy volunteers after a single oral dose of sulphamethoxazole. *Br J Clin Pharmacol* 1995; **39:** 621–5.
4. Mitra AK, *et al.* Inhibition of sulfamethoxazole hydroxylamine formation by fluconazole in human liver microsomes and healthy volunteers. *Clin Pharmacol Ther* 1996; **59:** 332–40.
5. Gill HJ, *et al.* The effect of fluconazole and ketoconazole on the metabolism of sulphamethoxazole. *Br J Clin Pharmacol* 1996; **42:** 347–53.
6. van der Ven AJAM, *et al.* Adverse reactions to co-trimoxazole in HIV infection. *Lancet* 1991; **338:** 431–3.
7. ter Hofstede HJM, *et al.* Drug reactions to cotrimoxazole in HIV infection: possibly not due to the hydroxylamine metabolites of sulphamethoxazole. *Br J Clin Pharmacol* 1999; **47:** 571–3.
8. Torgovnick J, Arsura E. Desensitization to sulfonamides in patients with HIV infection. *Am J Med* 1990; **88:** 548–9.

Porphyria. Sulfonamides have been associated with acute attacks of porphyria and are considered unsafe in porphyric patients.

Pregnancy. Some sulfonamides have been shown to cause fetal abnormalities including cleft palate in *animals*, but fears of teratogenic effects in humans do not appear to be substantiated. Sulfonamides are probably safe in the first trimester of pregnancy, although throughout pregnancy they should be used only in the absence of a suitable alternative drug.[1] Sulfonamides may displace serum-bound bilirubin and they should be avoided close to delivery because of the risk of kernicterus in the neonate. The risk of drug-induced bilirubin displacement has been reviewed.[2] The initial evidence suggesting a kernicterus-promoting effect of drugs in neonates was reported for sulfafurazole, and this drug now serves as a standard displacing agent against which other drugs are evaluated. Although all sulfonamides are highly protein bound, each has a different capacity to displace bilirubin. Sulfadiazine and sulfanilamide have been found to be the least displacing of the sulfonamides and the effects of sulfadiazine on bilirubin may not be clinically significant; an increased incidence of hyperbilirubinaemia and kernicterus has not been shown after use for prophylaxis of rheumatic fever during pregnancy. Sulfasalazine should theoretically cause significant bilirubin displacement, but studies suggest that the drug may be given to patients with Crohn's disease who are pregnant or breast feeding. Metabolites of sulfonamides have also been evaluated for kernicterus-promoting effects; glucuronide metabolites are expected to compete for binding sites less effectively than the parent compound, whereas acetylated metabolites of some sulfonamides appear to be more potent bilirubin displacers.

1. Wise R. Prescribing in pregnancy: antibiotics. *BMJ* 1987; **294:** 42–4.
2. Walker PC. Neonatal bilirubin toxicity: a review of kernicterus and the implications of drug-induced bilirubin displacement. *Clin Pharmacokinet* 1987; **13:** 26–50.

Interactions

The action of sulfonamides may be antagonised by *p*-aminobenzoic acid and its derivatives, particularly potassium aminobenzoate and the procaine group of local anaesthetics.

Sulfamethoxazole and other sulfonamides may potentiate the effects of some drugs, such as oral anticoagulants (p.1428), methotrexate (p.748), and phenytoin (p.498); this may be due to displacement of the drug from plasma protein binding sites or to inhibition of metabolism. However, the clinical significance of these interactions appears to depend on the particular sulfonamide involved. The possibility of interactions with other highly protein-bound drugs, such as NSAIDs, should be considered.

High doses of sulfonamides have been reported to have a hypoglycaemic effect; the antidiabetic effect of the sulfonylurea compounds may be enhanced by sulfonamides (p.462). Some sulfonamides have been associated with a decrease in plasma-ciclosporin concentrations when used together (p.1826). Isolated reports have described possible failures of hormonal contraceptives resulting in pregnancy in patients given sulfonamides (p.2068).

The use of compounds which render the urine acidic may increase the risk of crystalluria.

Antimicrobial Action

Sulfamethoxazole and other sulfonamides have a similar structure to *p*-aminobenzoic acid and interfere with the synthesis of nucleic acids in sensitive micro-organisms by blocking the conversion of *p*-aminobenzoic acid to the coenzyme dihydrofolic acid, a reduced form of folic acid; in man, dihydrofolic acid is obtained from dietary folic acid so sulfonamides do not affect human cells. Their action is primarily bacteriostatic, although they may be bactericidal where concentrations of thymine are low in the surrounding medium. The sulfonamides have a broad spectrum of action, but the development of widespread resistance (see below) has greatly reduced their usefulness, and susceptibility often varies widely even among nominally sensitive pathogens.

Gram-positive cocci, particularly the Group A streptococci and some strains of *Streptococcus pneumoniae*, are usually sensitive and staphylococci also demonstrate sensitivity but to a lesser extent. Enterococci and many of the clostridia are more or less resistant, although strains of *Clostridium perfringens* are moderately susceptible. Among other Gram-positive organisms that have been reported to be sensitive are *Bacillus anthracis* and many strains of Nocardia, especially *N. asteroides*.

The Gram-negative cocci *Neisseria meningitidis* and *N. gonorrhoeae* were formerly extremely susceptible to sulfonamides, but many strains are now resistant. Susceptibility is often seen in *Haemophilus influenzae* although resistance in *H. ducreyi* is increasingly common. Susceptibility varies widely among the Enterobacteriaceae: strains of *Escherichia coli*, *Klebsiella*, *Proteus*, *Salmonella*, and *Serratia* are sometimes sensitive, but few strains of *Shigella* are now susceptible. *Vibrio cholerae* may be sensitive.

Other organisms that have been reported to be sensitive include *Actinomyces* spp., *Brucella*, *Klebsiella granulomatis*, *Legionella*, and *Yersinia pestis*. Chlamydiaceae are sensitive, but not mycoplasmas, rickettsias, or spirochaetes, nor in general the mycobacteria. *Pseudomonas aeruginosa* is resistant, although sulfonamides may be effective against *Burkholderia pseudomallei* (*Pseudomonas pseudomallei*).

Sulfonamides have some activity against the protozoa *Plasmodium falciparum* and *Toxoplasma gondii*. They are also active against *Pneumocystis jirovecii*, but are ineffective against most fungi.

Sulfamethoxazole and other sulfonamides demonstrate synergy with the dihydrofolate reductase inhibitors pyrimethamine and trimethoprim which inhibit a later stage in folic acid synthesis. For reports of the antimicrobial activity of sulfamethoxazole with trimethoprim, see Co-trimoxazole, p.259.

The *in-vitro* antimicrobial activity of sulfamethoxazole is very dependent on both the culture medium and size of inoculum used.

Resistance. Acquired resistance to sulfonamides is common and widespread among formerly susceptible organisms, particularly *Neisseria* spp., *Shigella* and some other enterobacteria, staphylococci, and streptococci.

There appear to be several mechanisms of resistance including alteration of dihydropteroate synthetase, the enzyme inhibited by sulfonamides, to a less sensitive form, or an alteration in folate biosynthesis to an alternative pathway; increased production of *p*-aminobenzoic acid; or decreased uptake or enhanced metabolism of sulfonamides.

Resistance may result from chromosomal alteration, or may be plasmid-mediated and transferable, as in many resistant strains of enterobacteria. High-level resistance is usually permanent and irreversible. There is complete cross-resistance between the different sulfonamides.

Pharmacokinetics

Sulfamethoxazole is readily absorbed from the gastrointestinal tract and peak plasma concentrations are reached after about 2 hours. Following a single 2-g oral dose, blood concentrations of up to 100 micrograms/mL are achieved. About 70% is bound to plasma proteins. The plasma half-life is about 6 to 12 hours; it is prolonged in patients with severe renal impairment.

Sulfamethoxazole, like most sulfonamides, diffuses freely throughout the body tissues and may be detected in the urine, saliva, sweat, and bile, in the cerebrospinal, peritoneal, ocular, and synovial fluids, and in pleural and other effusions. It crosses the placenta into the fetal circulation and low concentrations have been detected in breast milk.

Sulfamethoxazole undergoes conjugation mainly in the liver, chiefly to the inactive N^4-acetyl derivative; this metabolite represents about 15% of the total amount of sulfamethoxazole in the blood. Metabolism is increased in patients with renal impairment and decreased in those with hepatic impairment. Elimination in the urine is dependent on pH. About 80 to 100% of a dose is excreted in the urine, of which about 60% is in the form of the acetyl derivative, with the remainder as unchanged drug and glucuronide.

Sulfamethoxazole is also oxidised to the hydroxylamine, a metabolite that has been implicated in adverse reactions to sulfonamides (see also Immunocompromised Patients, under Precautions, above), although some doubt has been cast upon this hypothesis.

Uses and Administration

The use of sulfamethoxazole and other sulfonamides has been limited by the increasing incidence of resistant organisms. Their main use has been in the treatment of acute, uncomplicated urinary-tract infections, particularly those caused by *Escherichia coli*. They have also been used in nocardiosis, and in some other bacterial infections such as otitis media, *Chlamydia* and *Chlamydophila* infections, and prophylaxis of meningococcal meningitis, but have largely been replaced by other drugs: even where pathogens retain some sensitivity to sulfonamides, a combination such as co-trimoxazole (sulfamethoxazole with trimethoprim) has often been preferred. The usual treatment of these infections is discussed under Choice of Antibacterial, p.162. Sulfonamides are also used, often with pyrimethamine or trimethoprim, in the treatment of protozoal infections, particularly malaria (p.594) and toxoplasmosis (p.826). They are also used similarly in pneumocystis pneumonia (p.521).

Sulfamethoxazole is an intermediate-acting sulfonamide that has been given orally in a usual dose of 2 g initially, followed by 1 g twice daily. In severe infections 1 g three times daily has been given.

Children have been given a dose of 50 to 60 mg/kg initially, followed by 25 to 30 mg/kg twice daily, up to a maximum daily dose of 75 mg/kg.

Reduction of dosage may be required in patients with renal impairment.

For the uses and dosage of sulfamethoxazole with trimethoprim, see Co-trimoxazole, p.259.

Sulfamethoxazole lysine has also been used.

Administration. US licensed product information for a former product of sulfamethoxazole recommended that blood concentrations be measured in patients receiving sulfonamides for serious infections. The following concentrations of free sulfonamide in the blood were considered to be therapeutically effective:

- for most infections, 50 to 150 micrograms/mL
- for serious infections, 120 to 150 micrograms/mL

Concentrations of 200 micrograms/mL should not be exceeded since the incidence of adverse reactions might be increased.

Preparations

BP 2008: Co-trimoxazole Intravenous Infusion; Co-trimoxazole Oral Suspension; Co-trimoxazole Tablets; Dispersible Co-trimoxazole Tablets; Paediatric Co-trimoxazole Oral Suspension; Paediatric Co-trimoxazole Tablets; ***USP 31:*** Sulfamethoxazole and Trimethoprim Injection; Sulfamethoxazole and Trimethoprim Oral Suspension; Sulfamethoxazole and Trimethoprim Tablets; Sulfamethoxazole Oral Suspension; Sulfamethoxazole Tablets.

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Arg.:*** Adrenol; Bacti-Uril; Bacticel; Bactrim; Bactrim Balsamico; Cotrizol-G; Danferane; Diocla†; Dosulfin Bronquial; Dosulfin Fuerte; Enterobacticel; Netocur; Netocur Balsamico; Neumobacticel; Novidrine; Sulfagrand; Tritenk; Urisept NF; Uro-Bactrim†; ***Austral.:*** Bactrim; Cosig†; Resprim; Septrin; Trimoxazole; ***Austria:*** Bactrim; Cotribene; Eusaprim; Oecotrim; Trimetho comp; ***Belg.:*** Bactrim; Cotrim; Eusaprim; Steroprim†; ***Braz.:*** Assepium; Assepium Balsamico; Bac-Sulfitrin; Bacfar; Bacprotin; Bacris†; Bacteracin; Bactrim; Bactrisan; Bactrizol; Bactropin; Batrox; Baxapril†; Benectrin; Benectrin Balsamico; Binoctrin†; Clotrizol†; Diazol; Dientrin; Dispeptrin; Duoctrin†; Ectrin; Ectrin Balsamico; Espectrin†; Espectroprima†; Gamactrin; Imuneprim; Infectrin; Lifactrin†; Linurin†; Lupectrim†; Metoprin; Metoprin Balsamico; Neotrin; Pulkrin; Qiftrin†; Quimio-Ped†; Roytrin†; Selectrin; Selectrin Balsamico; Septiolan†; Teutrin; Tricban; Trimexazol; Trimezol†; Uro-Baxapril†; Uroctrin; Uropol; ***Canad.:*** Apo-Sulfatrim; Novo-Trimel; Nu-Cotrimox; Septra; ***Chile:*** Bacterol; Bactrimel; Entero Micinovo; Introcin†; Septrin; Trelibec; Uro-Micinovo; ***Cz.:*** Apo-Sulfatrim†; Berlocid†; Biseptol; Bismoral; Nopil†; Oriprim†; Primotren; Sumetrolim; Supracombin†; ***Denm.:*** Sulfotrim†; ***Fin.:*** Cotrim; ***Fr.:*** Bactrim; Eusaprim†; ***Ger.:*** Bactoreduct†; Berlocid; Cotrim; Cotrim-Diolan; Cotrim-Hefa; Cotrimhexal; Cotrimox-Wolff; Cotrimstada; Drylin; Eusaprim; Kepinol; Microtrim†; Sigaprim†; Supracombin†; TMS; ***Gr.:*** Bactrimel; Bioprim†; Septrin; ***Hong Kong:*** Chemitrim†; Chemoprim; Cotrim; Dhatrin; Letus; Septrin; ***Hung.:*** Cotripharm; Sumetrolim; ***India:*** Bactrim; Ciplin; Colizole; Cotrimol†; Oriprim; Pyramet; Sepmax; Septran; Tabrol; Trisulfose; ***Indon.:*** Bactoprim Combi; Bactricid; Bactrim; Bactrizol; Cotrim; Cotrimol; Dumotrim; Erphatrim; Ikaprim; Infatrim; Kaftrim; Lapikot; Licoprima; Meditrim; Meprotrin; Nufaprim; Ottoprim; Primadex; Primazole; Primsulfon; Sanprima; Septrin; Spectrem; Sulprim; Sultrimmix; Trimezol; Triminex; Trimoxsul; Trixzol; Trizole; Ulfaprim; Wiatrim; Xepaprim; Zoltrim; Zultrop; ***Irl.:*** Duobact†; Septrin; ***Israel:*** Diseptyl; Resprim; Septrin; ***Ital.:*** Abacin†; Bactrim; Chemitrim; Eusaprim; Gantrim†; ***Jpn:*** Bactramin; ***Malaysia:*** Bacin; Baserin†; Chemix; Cotrim; Resprim; Trimexazole; Virin†; ***Mex.:*** Andoprim; Anitrim; Apo-Trinelax; Bacpiryl; Bactelan; Bacteric; Bactide; Bactilen; Bactiver;

Bactrim; Bactrim Compositum; Bactropin; Bateral; Batrizol; Bioprim; Bisultrim; Brogamax; Dertrin; Dibaprim; Ectaprim; Esteprim; Eutrim; Fartropin; Fectri; Guayaprin; Kaltrim; Maxtrim; Metoxiprim; Microbactim†; Mixange; Octex; Octiban; Pisatrina; Polibatrin; Pribac; Protaxol; Protrim; Sadocin; Septrin; Servitrim; Soltrim; Sulfawal; Sulfoid Trimetho; Sulfort; Sulprim; Sultiprim†; Syraprim†; Thriazol; Tribakin; Trime/Sulfa†; Trimetoger; Trimetox; Trimexazol; Trimexole; Trimexole Compositum; Trimzol; Trinelax†; Trisufin†; Vanadyl; ***Neth.:*** Bactrimel; Eusaprim†; Sulfotrim; ***Norw.:*** Bactrim; Trimetoprim-Sulfa†; ***NZ:*** Apo-Sulfatrim; Trisul; ***Philipp.:*** Bacidal; Bactille; Bactrim; Bacxal; Baczole; Bantizol; Chromo-Z; Combi-Methoxan; Costazole; Cozole; Drilozole; Fedimed; Forteprim; Globaxol; Ivatrim; Kassemox; Lictora; Macromed; Moxadden; Moxzole; Neotrim; Onetrim; Oprizole; Prizogen; Procor; Renatrim; Rimezone; Rotrace; Scribcin; Septrin; Suprex; Syltrifil; Synermed; Triforam; Trim-S; Trimephar; Trimocom; Trimoxis; Triphimox; Trizole; Xanazole; Zamboprim; Zolmed; ***Pol.:*** Bactrim; Biseptol; Groseptol†; Septrin; Two-Septol; ***Port.:*** Bactrim; Cotrim†; Metomide†; Microcetim; Septrin; ***Rus.:*** Biseptol (Бисептол); Oriprim (Ориприм); Rancotrim (Ранкотрим); ***S.Afr.:*** Acuco; Bactrim; Bencole; Casicot; Cocydal; Cozole; Durobac; Fabubac†; Lagatrim; Meditrim; Mezenol†; Purbac; Septran; Spectrim; Trimethox; Trimzol; Xerazole; Xeroprim†; ***Singapore:*** Apo-Sulfatrim; Bacin; BS†; Chemix; Chemoprim; Co-Trimexazole; Dhatrin; Septrin†; Suprim; Trimaxazole; Trimezole†; ***Spain:*** Bactopumon; Balsoprim; Bronco Aseptilex Fuerte; Broncomega†; Broncovir; Bronquicisteina; Bronquidiazina CR; Bronquimar; Bronquimucil†; Busetal†; Cotrazol; Eduprim Mucolitico; Eduprim†; Gobens Trim; Momentol; Neumopectolina†; Pulmo Menal†; Pulmosterin Duo; Septrin; Soltrim; ***Swed.:*** Bactrim; Eusaprim; ***Switz.:*** Agoprim†; Bactrim; Cotrim; Escoprim; Groprim; Lagatrim; Mediprim; Nopil; Sigaprim†; Supracombin†; ***Thai.:*** Actin; Bacin; Bacta†; Bactrim; Baczole; Chemoprim†; Co-Tasian; Co-Trimed; Conprim; Cotamox; Ko-Cap; Ko-Kure; Ladar; Lastrim; Letus; M-Trim; Mano-Trim; Med-Sultrim†; Mega-Prim; Metrim; Metxaprim; Mycosamthong; Po-Trim; Pulvicin†; Septrin†; Spectrim; Sulbacta; Sulfomeith; Suntrim; Tampo†; Toprim†; Trimexazole; Triprim; Trixzol; Zoleprim†; ***Turk.:*** Bactrim; Bakton; Kemoprim; Metoprim; Mikrosid; Septrin; Trifen; Trimoks; ***UAE:*** Trimol; ***UK:*** Fectrim; Septrin; ***USA:*** Bactrim; Cotrim; Septra; SMZ-TMP; Sulfatrim; ***Venez.:*** Bactrimel; Bactron†; Co-Sultrin; Forcrim; Trimecor; Trimetoprim Sulfa†; Tripur.

Sulfamethoxypyridazine *(BAN, rINN)*

Solfametossipiridazina; Sulfamethoxypyridazin; Sulfaméthoxypyridazine; Sulfamethoxypyridazinum; Sulfamethoxypyridazinum ad usum veterinarium; Sulfametoksipyridatsiini; Sulfametoxipiridazina; Sulfametoxipyridazin; Sulphamethoxypyridazine; Szulfametoxipiridazin. N^1-(6-Methoxypyridazin-3-yl)sulphanilamide.

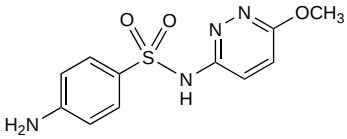
Сульфаметоксипиридазин

$C_{11}H_{12}N_4O_3S$ = 280.3.

CAS — 80-35-3.

ATC — J01ED05.

ATC Vet — QJ01EQ15.



Pharmacopoeias. In *Int.* and *Viet.* In *Eur.* (see p.vii) for veterinary use only.

Ph. Eur. 6.2 (Sulfamethoxypyridazine for Veterinary Use; Sulfametoxypyridazine BP(Vet) 2008). A white or slightly yellowish crystalline powder which colours slowly on exposure to light. Practically insoluble in water; slightly soluble in alcohol; sparingly soluble in acetone; very slightly soluble in dichloromethane; dissolves in dilute mineral acids and solutions of alkali hydroxides. Protect from light.

Profile

Sulfamethoxypyridazine is a long-acting sulfonamide with properties similar to those of sulfamethoxazole (p.340) and has been used for the treatment of susceptible infections. It is rapidly absorbed from the gastrointestinal tract and excreted slowly in urine, partly as the N^4-acetyl metabolite; it remains detectable for up to 7 days after a dose. It has also been used with trimethoprim similarly to co-trimoxazole.

Acetyl sulfamethoxypyridazine, which is hydrolysed in the gastrointestinal tract forming sulfamethoxypyridazine, and sulfamethoxypyridazine sodium have also been used.

Skin disorders. Reference to the use of sulfamethoxypyridazine in the treatment of pemphigoid.[1] Sulfamethoxypyridazine has also been used in the treatment of dermatitis herpetiformis.[2]

1. Thornhill M, *et al.* An open clinical trial of sulphamethoxypyridazine in the treatment of mucous membrane pemphigoid. *Br J Dermatol* 2000; **143:** 117–26.
2. Fry L. Dermatitis herpetiformis. *Baillieres Clin Gastroenterol* 1995; **9:** 371–93.

Preparations

Proprietary Preparations (details are given in Part 3)

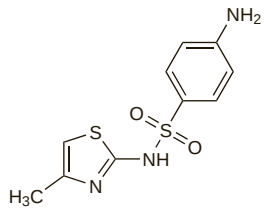
Multi-ingredient: ***Braz.:*** Urofen†; Uropac.

Sulfamethylthiazole

Methylsulfathiazole; Sulfametiltiazol. 4-Amino-*N*-(4-methyl-2-thiazolyl)benzenesulfonamide.

$C_{10}H_{11}N_3O_2S_2$ = 269.3.

CAS — 515-59-3.



Profile

Sulfamethylthiazole is a sulfonamide with properties similar to those of sulfamethoxazole (p.340). It is applied topically with tetracycline in the treatment of eye infections.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Ital.:*** Pensulvit.

Sulfametopyrazine *(BAN)*

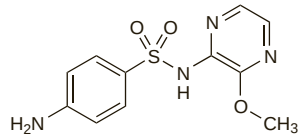
Sulfalene *(USAN, pINN)*; AS-18908; NSC-110433; Solfametopirazina; Solfametossipirazina; Sulfaleeni; Sulfalen; Sulfalène; Sulfaleno; Sulfalenum; Sulfamethoxypyrazine; Sulfapirazinmetossina; Sulfapyrazin Methoxyne; Sulphalene. N^1-(3-Methoxypyrazin-2-yl)sulphanilamide.

Сульфален

$C_{11}H_{12}N_4O_3S$ = 280.3.

CAS — 152-47-6.

ATC — J01ED02.



Pharmacopoeias. In *It.*

Adverse Effects, Treatment, and Precautions

As for Sulfamethoxazole, p.340.

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

Interactions

As for Sulfamethoxazole, p.341.

Antimicrobial Action

As for Sulfamethoxazole, p.341.

Pharmacokinetics

Sulfametopyrazine is readily absorbed from the gastrointestinal tract; 60 to 80% is bound to plasma proteins. Only about 5% of a dose is metabolised to the acetyl derivative. It is slowly excreted in the urine. The biological half-life has been reported to be about 60 to 65 hours.

Uses and Administration

Sulfametopyrazine is a long-acting sulfonamide that has been used orally in the treatment of respiratory- and urinary-tract infections due to sensitive organisms.

Sulfametopyrazine is given with pyrimethamine (p.611) in the treatment of malaria.

It has also been given in the ratio 4 parts of sulfametopyrazine to 5 parts of trimethoprim as a combination with uses similar to those of co-trimoxazole (p.259).

Preparations

Proprietary Preparations (details are given in Part 3)

Ger.: Longum†.

Multi-ingredient: ***Belg.:*** Co-Arinate; Dafrafin; ***Ital.:*** Metakelfin; ***Mex.:*** Kelfiprim†.

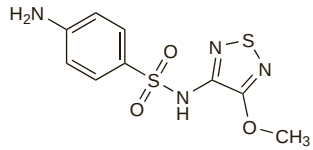
Sulfametrole *(BAN, rINN)*

Sulfametrol; Sulfamétrole; Sulfametrolum. N^1-(4-Methoxy-1,2,5-thiadiazol-3-yl)sulphanilamide.

Сульфаметрол

$C_9H_{10}N_4O_3S_2$ = 286.3.

CAS — 32909-92-5.



Profile

Sulfametrole is a sulfonamide with properties similar to those of sulfamethoxazole (p.340). It is given in the ratio of 5 parts of sulfametrole to 1 part of trimethoprim as a combination with uses similar to those of co-trimoxazole (p.259). Usual oral doses are 960 mg (800 mg of sulfametrole and 160 mg of trimethoprim) twice daily. It has also been given as the sodium salt by intravenous infusion.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Austria:*** Lidaprim; ***Gr.:*** Lidaprim; ***Hong Kong:*** Lidaprim; ***Ital.:*** Lidaprim†; ***Neth.:*** Lidatrim; ***Rus.:*** Lidaprim (Лидаприм); ***Thai.:*** Lidaprim†.

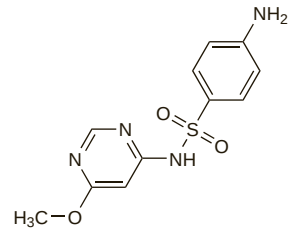
Sulfamonomethoxine *(BAN, USAN, rINN)*

DJ-1550; DS-36; ICI-32525; Ro-4-3476; Sulfamonométhoxine; Sulfamonomethoxinum; Sulfamonometoxina. N^1-(6-Methoxypyrimidin-4-yl)sulphanilamide monohydrate.

Сульфамонометоксин

$C_{11}H_{12}N_4O_3S,H_2O$ = 298.3.

CAS — 1220-83-3 (anhydrous sulfamonomethoxine).



(anhydrous sulfamonomethoxine)

Pharmacopoeias. In *Jpn.*

Profile

Sulfamonomethoxine is a sulfonamide antibacterial with properties similar to those of sulfamethoxazole (p.340). It is used in veterinary medicine.

Sulfamoxole *(BAN, USAN, rINN)*

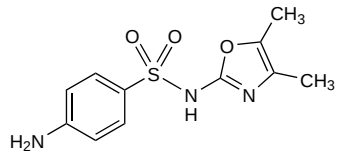
Sulfamoksoli; Sulfamoxol; Sulfamoxolum; Sulphadimethyloxazole; Sulphamoxole. N^1-(4,5-Dimethyloxazol-2-yl)sulphanilamide.

Сульфамоксол

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

CAS — 729-99-7.

ATC — J01EC03.



NOTE. Compounded preparations of sulfamoxole may be represented by the following name:

- Co-trifamole (*BAN*)—sulfamoxole 5 parts and trimethoprim 1 part (see p.257).

Pharmacopoeias. In *Fr.*

Profile

Sulfamoxole is a sulfonamide antibacterial with properties similar to those of sulfamethoxazole (p.340). It has been used with trimethoprim as co-trifamole (p.257).

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***S.Afr.:*** Supristol†.