2. Krcmery S, *et al.* Treatment of lower urinary tract infection in pregnancy. *Int J Antimicrob Agents* 2001; **17:** 279–82.
3. Wing DA. Pyelonephritis in pregnancy: treatment options for optimal outcomes. *Drugs* 2001; **61:** 2087–96.
4. Smaill F. Antibiotics for asymptomatic bacteriuria in pregnancy. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2001 (accessed 16/05/05).
5. Mittal P, Wing DA. Urinary tract infections in pregnancy. *Clin Perinatol* 2005; **32:** 749–64.
6. Macejko AM, Schaeffer AJ. Asymptomatic bacteriuria and symptomatic urinary tract infections during pregnancy. *Urol Clin North Am* 2007; **34:** 35–42.
7. Smaill F, Vazquez JC. Antibiotics for asymptomatic bacteriuria in pregnancy. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2007 (accessed 07/08/08).


**Women.** References to urinary-tract infections in women and their management.


1. Warren JW, *et al.* Guidelines for antimicrobial treatment of uncomplicated acute bacterial cystitis and acute pyelonephritis in women. *Clin Infect Dis* 1999; **29:** 745–58.
2. Hooton TM. Recurrent urinary tract infection in women. *Int J Antimicrob Agents* 2001; **17:** 259–68.
3. Fihn SD. Acute uncomplicated urinary tract infection in women. *N Engl J Med* 2003; **349:** 259–66.
4. Milo G, *et al.* Duration of antibacterial treatment for uncomplicated urinary tract infection in women. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2005 (accessed 07/08/08).
5. Nicolle L, *et al.* Uncomplicated urinary tract infection in women: current practice and the effect of antibiotic resistance on empiric treatment. *Can Fam Physician* 2006; **52:** 612–8.
6. Foster RT. Uncomplicated urinary tract infections in women. *Obstet Gynecol Clin North Am* 2008; **35:** 235–48.
7. André M, Mölstad S. Nya riktlinjer för urinvägsinfektion hos kvinnor. *Lakartidningen* 2008; **105:** 1107–9.


### Whipple's disease

Whipple's disease is a rare chronic systemic condition associated with infection with *Tropheryma whippelii*.[1-4] It was once considered to be a disease predominantly involving the small intestine and resulting in malabsorption, but may affect virtually all organs. There is probably CNS involvement in all patients with Whipple's disease, although it may only be evident in 10 to 20%. Before the use of antibacterial therapy the disease was invariably fatal. The treatment generally recommended is either benzylpenicillin (sometimes given as procaine benzylpenicillin) and streptomycin, or ceftriaxone, parenterally for two weeks, followed by co-trimoxazole orally for at least one year.[2,3,5,6] Such long-term treatment with co-trimoxazole, a drug that crosses the blood-brain barrier, is advisable because of the relatively high frequency and seriousness of CNS relapse. These relapses respond less well to antibacterial treatment; chloramphenicol has been used in those not responding to the above regimen and a patient with CNS relapse improved on ceftriaxone given intravenously.[7] Further alternatives may be a tetracycline[8] or cefixime.[6] A patient intolerant of co-trimoxazole was given phenoxymethylpenicillin and probenecid after the initial 14-day course of benzylpenicillin and streptomycin.[9] There has also been a report of benefit in a penicillin-allergic patient treated with erythromycin.[10] A combination of doxycycline with hydroxychloroquine may be tried in patients without neurological involvement.[3]


1. Relman DA, *et al.* Identification of the uncultured bacillus of Whipple's disease. *N Engl J Med* 1992; **327:** 293–301.
2. Marth T, Raoult D. Whipple's disease. *Lancet* 2003; **361:** 239–46.
3. Fenollar F, *et al.* Whipple's disease. *N Engl J Med* 2007; **356:** 55–66.
4. Schneider T, *et al.* Whipple's disease: new aspects of pathogenesis and treatment. *Lancet Infect Dis* 2008; **8:** 179–90.
5. Singer R. Diagnosis and treatment of Whipple's disease. *Drugs* 1998; **55:** 699–704.
6. Maiwald M, Relman DA. Whipple's disease and Tropheryma whippelii: secrets slowly revealed. *Clin Infect Dis* 2001; **32:** 457–63.
7. Adler CH, Galetta SL. Oculo-facial-skeletal myorhythmia in Whipple disease: treatment with ceftriaxone. *Ann Intern Med* 1990; **112**: 467–9.
8. Abramowicz M, ed. The choice of antibacterial drugs. In: *Handbook of antimicrobial therapy.* 18th ed. New Rochelle NY: The Medical Letter, 2008: 72.
9. Rickman LS, *et al.* Brief report: uveitis caused by Tropheryma whippelii (Whipple's bacillus). *N Engl J Med* 1995; **332:** 363–6.
10. Bowles KM, *et al.* A 35-year-old with swollen knees who had recurrent fever and pericarditis, then diarrhoea before getting better. *Lancet* 1996; **348:** 1356.


### Yaws

See under Syphilis, p.192.

### Yersinia enteritis

See p.174.

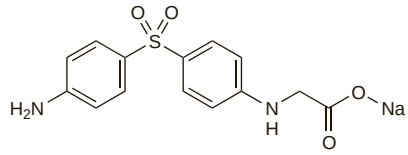
## Acediasulfone Sodium *(rINN)*

Acediasulfona sódica; Acédiasulfone Sodique; Acediasulfonnatrium; Acediasulfonum Natricum; Asediasulfoninatrium; Sodium Diaphenylsulphonacetate. *N-p*-Sulphanilylphenylglycine sodium.

Ацедиасульфон Натрий

$C_{14}H_{13}N_2NaO_4S$ = 328.3.

*CAS — 127-60-6.*



### Profile

Acediasulfone sodium is reported to have antibacterial properties and is an ingredient of preparations used topically in the treatment of local infections of the ear.

### Preparations

**Proprietary Preparations** (details are given in Part 3)

**Multi-ingredient:** ***Austria:*** Ciloprin cum Anaesthetico†; ***Fin.:*** Ciloprin cum Anaesthetico†; ***India:*** Otogesic; ***Switz.:*** Ciloprin ca†.

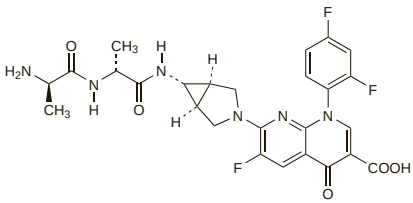
## Alatrofloxacin Mesilate *(rINNM)*

Alatrofloxacin Mesylate *(USAN)*; Alatrofloxacine, Mésilate d'; Alatrofloxacini Mesilas; CP-116517-27; Mesilato de alatrofloxacino. 7-{(1*R*,5*S*,6*s*)-6-[(*S*)-2-((*S*)-2-Aminopropionamido)propionamido]-3-azabicyclo[3.1.0]hex-3-yl}-1-(2,4-difluorophenyl)-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid monomethanesulphonate.

Алатрофлоксацина Мезилат

$C_{26}H_{25}F_3N_6O_5,CH_3SO_3H$ = 654.6.

*CAS — 157182-32-6 (alatrofloxacin); 157605-25-9 (alatrofloxacin mesilate).*



*(alatrofloxacin)*

### Profile

Alatrofloxacin is a prodrug of the fluoroquinolone antibacterial trovafloxacin (p.357) and has been used intravenously as the mesilate in the treatment of susceptible infections.

Alatrofloxacin and trovafloxacin preparations were withdrawn worldwide after reports of unpredictable severe hepatic adverse effects, including some fatalities.

### Preparations

**Proprietary Preparations** (details are given in Part 3)

***Canad.:*** Trovan†; ***USA:*** Trovan†.

# Amikacin *(BAN, rINN)*

Amicacina; Amikacina; Amikacinas; Amikacine; Amikacinum; Amikacyna; Amikasiini. 6-*O*-(3-Amino-3-deoxy-α-D-glucopyranosyl)-4-*O*-(6-amino-6-deoxy-α-D-glucopyranosyl)-*N*$^1$-[(2*S*)-4-amino-2-hydroxybutyryl]-2-deoxystreptamine.

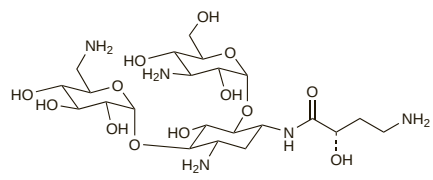
Амикацин

$C_{22}H_{43}N_5O_{13}$ = 585.6.

*CAS — 37517-28-5.*

*ATC — D06AX12; J01GB06; S01AA21.*

*ATC Vet — QD06AX12; QJ01GB06; QS01AA21.*



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

**Ph. Eur. 6.2** (Amikacin). An antimicrobial substance obtained from kanamycin A. A white or almost white powder. Sparingly soluble in water; practically insoluble in alcohol and in acetone; slightly soluble in methyl alcohol. A 1% solution in water has a pH of 9.5 to 11.5.

**USP 31** (Amikacin). A white crystalline powder. Sparingly soluble in water. pH of a 1% solution in water is between 9.5 and 11.5. Store in airtight containers.

### Amikacin Sulfate *(USAN, rINNM)*

Amikacin Sulphate *(BANM)*; Amikacin-disulfát; Amikacine, sulfate d'; Amikacini Disulfas; Amikacini sulfas; Amikacino sulfatas; Amikacinsulfat; Amikacin-szulfát; Amikacyny siarczan; Amikasiinisulfaatti; Amikasin Sülfat; BB-K8; Sulfato de amikacina.

Амикацина Сульфат

$C_{22}H_{43}N_5O_{13},2H_2SO_4$ = 781.8.

*CAS — 39831-55-5.*

*ATC — D06AX12; J01GB06; S01AA21.*

*ATC Vet — QD06AX12; QJ01GB06; QS01AA21.*

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

**Ph. Eur. 6.2** (Amikacin Sulphate). A white or almost white powder. It loses not more than 13.0% of its weight on drying. Freely soluble in water; practically insoluble in alcohol and in acetone. The pH of a 1% solution in water is between 2.0 and 4.0. Store in airtight containers.

**USP 31** (Amikacin Sulfate). Amikacin sulfate having a molar ratio of amikacin to $H_2SO_4$ of 1:2 contains the equivalent of not less than 674 micrograms and not more than 786 micrograms of amikacin per mg, calculated on the dried basis. Amikacin sulfate having a molar ratio of amikacin to $H_2SO_4$ of 1:1.8 contains the equivalent of not less than 691 micrograms and not more than 806 micrograms of amikacin per mg, calculated on the dried basis.

A white crystalline powder. Freely soluble in water. pH of a 1% solution in water is between 2.0 and 4.0 (1:2 salt) and 6.0 to 7.3 (1:1.8 salt). Store in airtight containers.

**Incompatibility.** For discussion of the incompatibility of aminoglycosides, including amikacin, with beta lactams, see under Gentamicin Sulfate, p.282. Amikacin is also reported to be incompatible with various other drugs. However, reports are contradictory in many cases, and other factors, such as the strength and composition of the vehicles used, may play a role.

**Stability.** Solutions may darken from colourless to pale yellow but this does not indicate a loss of potency.

### Adverse Effects, Treatment, and Precautions

As for Gentamicin Sulfate, p.282. Peak plasma concentrations of amikacin greater than 30 to 35 micrograms/mL or trough concentrations greater than 5 to 10 micrograms/mL should be avoided. Amikacin affects auditory (cochlear) function to a greater extent than gentamicin.

**Effects on the eyes.** A report of retinal damage after intravitreal injection of amikacin.[1]


1. Jackson TL, Williamson TH. Amikacin retinal toxicity. *Br J Ophthalmol* 1999; **83:** 1199–1200.


### Interactions

As for Gentamicin Sulfate, p.283.

### Antimicrobial Action

As for Gentamicin Sulfate, p.283. Amikacin is active against a similar range of organisms although it is also reported to have some activity against *Nocardia asteroides*, *Mycobacterium tuberculosis*, and some atypical mycobacterial strains. Amikacin is not degraded by many of the common enzymes often responsible for acquired aminoglycoside resistance. In consequence, cross-resistance with gentamicin and other aminoglycosides is infrequent and amikacin may be effective against strains resistant to other aminoglycosides. However, resistant strains of Gram-negative bacteria and staphylococci have been reported, and it is generally reserved for infections resistant to other aminoglycosides, although reports differ as to the extent and speed of the development of amikacin resistance where it has been widely used.

◊ References.


1. Ho YII, *et al.* In-vitro activities of aminoglycoside-aminocyclitols against mycobacteria. *J Antimicrob Chemother* 1997; **40:** 27–32.


### Pharmacokinetics

As for Gentamicin Sulfate, p.284.

On intramuscular injection, peak plasma-amikacin concentrations of about 20 micrograms/mL are achieved 1 hour after a 500-mg dose, reducing to about

2 micrograms/mL 10 hours after injection. A plasma concentration of 38 micrograms/mL has been reported after the intravenous infusion of 500 mg over 30 minutes, reducing to 18 micrograms/mL 1 hour later. Amikacin has been detected in body tissues and fluids after injection; it crosses the placenta but does not readily penetrate into the CSF, although substantial penetration of the blood-brain barrier has been reported in children with meningitis.

A plasma half-life of about 2 to 3 hours has been reported in patients with normal renal function. Most of a dose is excreted by glomerular filtration in the urine within 24 hours.

◊ References.


1. Vanhaeverbeek M, *et al*. Pharmacokinetics of once-daily amikacin in elderly patients. *J Antimicrob Chemother* 1993; **31:** 185–7.
2. Gaillard J-L, *et al*. Cerebrospinal fluid penetration of amikacin in children with community-acquired bacterial meningitis. *Antimicrob Agents Chemother* 1995; **39:** 253–5.
3. Bressolle F, *et al*. Population pharmacokinetics of amikacin in critically ill patients. *Antimicrob Agents Chemother* 1996; **40:** 1682–9.
4. Canis F, *et al*. Pharmacokinetics and bronchial diffusion of single daily dose amikacin in cystic fibrosis patients. *J Antimicrob Chemother* 1997; **39:** 431–3.
5. Tod M, *et al*. Population pharmacokinetic study of amikacin administered once or twice daily to febrile, severely neutropenic adults. *Antimicrob Agents Chemother* 1998; **42:** 849–56.
6. Tréluyer JM, *et al*. Nonparametric population pharmacokinetic analysis of amikacin in neonates, infants, and children. *Antimicrob Agents Chemother* 2002; **46:** 1381–7.


## Uses and Administration

Amikacin is a semisynthetic aminoglycoside antibiotic derived from kanamycin and is used similarly to gentamicin (p.284) in the treatment of severe Gram-negative and other infections. It is given as the sulfate, and is generally reserved for the treatment of severe infections caused by susceptible bacteria that are resistant to gentamicin and tobramycin. Amikacin has also been given with antimycobacterials in the treatment of nontuberculous mycobacterial infections (p.181). As with gentamicin, amikacin may be used with penicillins and with cephalosporins; the injections should be given at separate sites.

Doses of amikacin sulfate are expressed in terms of amikacin base; 1.3 g of amikacin sulfate is equivalent to about 1 g of amikacin. Adults and children may be given 15 mg/kg daily in equally divided doses every 8 or 12 hours by intramuscular injection. In life-threatening infections, the dose may be increased in adults up to a maximum of 500 mg every 8 hours. A dose of 7.5 mg/kg daily in two divided doses (equivalent to 250 mg twice daily in adults) may be given for the treatment of uncomplicated urinary-tract infections. The same doses may be given by slow intravenous injection over 2 to 3 minutes, or by intravenous infusion. In adults, 500 mg in 100 to 200 mL of diluent has been infused over 30 to 60 minutes; proportionately less fluid should be given to children.

Neonates may be given 10 mg/kg as a loading dose, followed by 15 mg/kg daily in two divided doses. If given by intravenous infusion, an infusion period of 1 to 2 hours is recommended. It has been suggested that doses may need to be adjusted in preterm neonates.

Treatment should preferably not continue for longer than 7 to 10 days, and the total dose given to adults should not exceed 15 g. Peak plasma concentrations greater than 30 to 35 micrograms/mL or trough plasma concentrations greater than 5 to 10 micrograms/mL should be avoided. Dosage should be adjusted in all patients according to plasma-amikacin concentrations, and this is particularly important where factors such as age, renal impairment, or prolonged therapy may predispose to toxicity, or where there is a risk of subtherapeutic concentrations. For discussion of the methods of calculating aminoglycoside dosage requirements, see Administration and Dosage, under Gentamicin, p.284. As with some other aminoglycosides, once-daily dosage has been used successfully with amikacin without increasing toxicity, but local guidelines should be consulted (see also Once-daily Dosage, p.285).

A 0.25% solution has been instilled into body cavities in adults.

A liposomal formulation of amikacin is under investigation.

### Preparations

***BP 2008:*** Amikacin Injection;
***USP 31:*** Amikacin Sulfate Injection.

**Proprietary Preparations** (details are given in Part 3)
***Arg.:*** Biklin; Greini; Riklinak; ***Austral.:*** Amikin; ***Austria:*** Biklin; ***Belg.:*** Amukin; ***Braz.:*** Amicacil†; Amicalin†; Amicilon; Aminocina†; Bactomicin†; Klebicil; Novamin; ***Canad.:*** Amikin†; ***Cz.:*** Amikin; Amikozit†; Miacin†; ***Fin.:*** Biklin; ***Fr.:*** Amiklin†; ***Ger.:*** Biklin; ***Gr.:*** Amicagel†; Amicasil; Amikan; Biorisan; Briklin; Cinegel; Durocin; Farcyclin; Flexelite; Fromentyl; Kancin-Gap; Lanomycin; Lifermycin; Likacin; Micalpha; Orlobin; Remikin; Roveniclin; Selaxa; Uzix; ***Hong Kong:*** Amikin; Apalin; Selemycin†; ***Hung.:*** Amikin; Likacin; ***India:*** Amcin; Amicin; Amicip; Mikacin; ***Indon.:*** Alostil; Amikin; Mikasin; ***Irl.:*** Amikin; ***Israel:*** Amikin†; ***Ital.:*** Amicasil; Amik; Amikan; BB-K8; Chemacin; Dramigel; Likacin; Lukadin; Mediamik; Migracin; Mikan; Mikavir; Nekacin; Pierami; ***Malaysia:*** Amikin†; Selemycin†; ***Mex.:*** Agnicin; Akacin; Amicina; Amikafur; Amikalem; Amikasons; Amikavi; Amikayect; Amikin; Amiyec; AMK; Baxi-K†; Beramikin; Biclin; Biokacin; Gamikal; Kafran; Kana; Karmikin; Libamic; Lisobac; Mikazul; Oprad; Plokim; Sermicina; Yectamid; ***Neth.:*** Amukin; ***NZ:*** Amikin; ***Philipp.:*** Amikacide; Amikin; Cidacid; Cinmik; Kamin; Kormakin; Nica; ***Pol.:*** Amikin; Biodacyna; ***Port.:*** Amic; Biclin; Kamina; ***Rus.:*** Amikozit (Амикозит); Selemycin (Селемицин); ***S.Afr.:*** Amikin; Kacinth-A; ***Singapore:*** Amikin; ***Spain:*** Biclin; Kanbine; ***Swed.:*** Biklin; ***Switz.:*** Amikin; ***Thai.:*** Akacin; Akicin; Amikasol†; Amikin; Anbikin; Siamik; Tipkin; Tybikin; ***Turk.:*** Amiketem; Amiklin; Amikozit; Mikasin; ***UAE:*** Mikacin; ***UK:*** Amikin; ***USA:*** Amikin; ***Venez.:*** Amikavax; Amikayect†; Behkacin; Biklin; Likacin.

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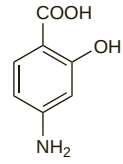
## Aminosalicylic Acid

Acidum Aminosalicylicum; Aminosalicílico, ácido; 4-Aminosalicylic Acid; Aminosalicylsyra; Aminosalisyylihappo; Aminosalylum; Para-aminosalicylic Acid; PAS; Pasalicylum. 4-Amino-2-hydroxybenzoic acid.

Аминосалициловая Кислота

$C_7H_7NO_3$ = 153.1.
*CAS — 65-49-6.*
*ATC — J04AA01.*
*ATC Vet — QJ04AA01.*




NOTE. Distinguish from 5-aminosalicylic acid (Mesalazine, p.1745).

**Pharmacopoeias.** In *US*.
**USP 31** (Aminosalicylic Acid). A white or practically white, bulky powder that darkens on exposure to light and air; it is odourless or has a slight acetous odour. Slightly soluble in water and in ether; soluble in alcohol; practically insoluble in benzene. Under no circumstances should a solution be used if its colour is darker than that of a freshly prepared solution. pH of a saturated solution in water is between 3.0 to 3.7. Store in airtight containers at a temperature not exceeding 30°. Protect from light.

## Calcium Aminosalicylate

Aminosalicilato cálcico; Aminosalicylate calcium; Aminosalylcalcium; Aminosalylkalcium; Aminosalyylikalsium; Calcii Aminosalicylas; Calcii Para-aminosalicylas; Calcium PAS; Kalciumaminosalicylat; Kalsiumaminosalisylaatti. Calcium 4-amino-2-hydroxybenzoate trihydrate.

Аминосалицилат Кальция

$(C_7H_6NO_3)_2Ca,3H_2O$ = 398.4.
*CAS — 133-15-3 (anhydrous calcium aminosalicylate).*
*ATC — J04AA03.*
*ATC Vet — QJ04AA03.*

**Pharmacopoeias.** *Jpn* includes the heptahydrate.

## Sodium Aminosalicylate

Aminosalicilato sódico; Aminosalicylan sodný dihydrát; Aminosalicylate Sodium; Aminosalylnatrium; Monosodium 4-Aminosalicylate Dihydrate; Natrii Aminosalicylas; Natrii aminosalicylas dihydricus; Natrii Paraaminosalicylas; Natrii Para-aminosalicylas; Natrio aminosalicilatas dihidratas; Natriumaminosalicylat; Natriumaminosalicylatdihydrat; Natriumaminosalisylaatti; Natriumaminosalisylaattidihydraatti; Pasalicylum Solubile; Sodium (aminosalicylate de) dihydraté; Sodium Para-aminosalicylate; Sodium PAS; Sodu aminosalicylan. Sodium 4-amino-2-hydroxybenzoate dihydrate.

Аминосалицилат Натрия

$C_7H_6NNaO_3,2H_2O$ = 211.1.
*CAS — 133-10-8 (anhydrous sodium aminosalicylate); 6018-19-5 (sodium aminosalicylate dihydrate).*
*ATC — J04AA02.*
*ATC Vet — QJ04AA02.*

**Pharmacopoeias.** In *Chin., Eur.* (see p.vii), and *US*.
**Ph. Eur. 6.2** (Sodium Aminosalicylate Dihydrate). A slightly hygroscopic, white or almost white, crystalline powder, or white or almost white crystals. Freely soluble in water; sparingly soluble in alcohol, practically insoluble in dichloromethane. A 2% solution in water has a pH of 6.5 to 8.5. Store in airtight containers. Protect from light.
**USP 31** (Aminosalicylate Sodium). A white to cream-coloured, practically odourless crystalline powder. Soluble 1 in 2 of water; sparingly soluble in alcohol; very slightly soluble in chloroform and in ether. Its solutions decompose slowly and darken in colour. Prepare solutions within 24 hours of use. Under no circumstances should a solution be used if its colour is darker than that of a freshly prepared solution. pH of a 2% solution in water is between 6.5 and 8.5. Store in airtight containers at a temperature not exceeding 40°. Protect from light.

**Stability.** Aqueous solutions of aminosalicylates are unstable and should be freshly prepared.

Solutions of sodium aminosalicylate in sorbitol or syrup degraded more quickly to *m*-aminophenol than those in glycerol or propylene glycol.[1] Colour developed in all solutions but was not found to be an accurate indicator of decomposition of sodium aminosalicylate as it reflected only oxidation of *m*-aminophenol.


1. Blake MI, *et al*. Effect of vehicle on the stability of sodium aminosalicylate in liquid dosage forms. *Am J Hosp Pharm* 1973; **30:** 441–3.


### Adverse Effects and Treatment

Aminosalicylic acid and its salts may cause the adverse effects of salicylates (see Aspirin, p.20).

Gastrointestinal effects are common and include nausea, vomiting, and diarrhoea; they may be reduced by giving doses with food or with an antacid but occasionally may be severe enough that therapy has to be withdrawn. Alteration of gastrointestinal function may lead to malabsorption of vitamin $B_{12}$, folate, and lipids.

Hypersensitivity reactions have been reported in 5 to 10% of adults, usually during the first few weeks of treatment, and include fever, skin rashes; less commonly, arthralgia, lymphadenopathy, and hepatosplenomegaly may occur and, rarely, a syndrome resembling infectious mononucleosis. Other adverse effects which have been attributed to a hypersensitivity reaction to aminosalicylate include jaundice and encephalitis. Blood disorders reported include haemolytic anaemia in patients with G6PD deficiency, agranulocytosis, eosinophilia, leucopenia, and thrombocytopenia. Psychosis may occasionally occur. Prolonged treatment may induce goitre and hypothyroidism. Crystalluria may occur.

**Effects on the liver.** Drug-induced hepatitis occurred in 0.32% of 7492 patients receiving antituberculous drugs; aminosalicylic acid was the most common cause.[1]


1. Rossouw JE, Saunders SJ. Hepatic complications of antituberculous therapy. *Q J Med* 1975; **44:** 1–16.


### Precautions

Aminosalicylic acid and its salts should be used with great care in patients with hepatic or renal impairment and in patients with gastric ulcer. They should be given with caution to patients with G6PD deficiency. The sodium salt should be used with caution in patients with heart failure.

Aminosalicylates interfere with tests for glycosuria using copper reagents and for urobilinogen using Ehrlich's reagent.

**Breast feeding.** Small amounts of aminosalicylic acid are present in breast milk. A maximum concentration of 1.1 microgram/mL has been reported in the breast milk of a lactating woman 3 hours after a 4-g dose of aminosalicylic acid.[1]


1. Holdiness MR. Antituberculosis drugs and breast feeding. *Arch Intern Med* 1984; **144:** 1888.


**Pregnancy.** The use of aminosalicylic acid or its salts is not recommended in pregnant patients due to gastrointestinal intolerance.[1] In addition it has been noted that, a study published in 1964 suggested that first-trimester exposure may be associated with congenital defects although other studies had not found similar effects.[2]


1. Snider D. Pregnancy and tuberculosis. *Chest* 1984; **86:** 10S–13S.
2. Briggs GG, *et al*. *Drugs in pregnancy and lactation.* 7th ed. Philadelphia: Lippincott Williams and Wilkins, 2005: 59.


### Interactions

The adverse effects of aminosalicylates and salicylates may be additive. Probenecid may also increase toxicity by delaying renal excretion and enhancing plasma concentrations of aminosalicylate. The activity of aminosalicylic acid may be antagonised by ester-type local anaesthetics such as procaine.

### Antimicrobial Action

Aminosalicylic acid is bacteriostatic and is active against *M. tuberculosis*. Other mycobacteria are usually resistant. It has a relatively weak action compared with other antituberculous drugs. Resistance develops quickly if aminosalicylic acid is used alone.

◊ References.


1. Rengarajan J, *et al*. The folate pathway is a target for resistance to the drug para-aminosalicylic acid (PAS) in mycobacteria. *Mol Microbiol* 2004; **53:** 275–82.