Administration in children. Use of cycloserine is licensed in both the UK and USA for children, although age ranges are not specified in licensed product information. For the treatment of drug-resistant tuberculosis the American Academy of Pediatrics (AAP) suggests a dose of 5 to 10 mg/kg twice daily, to a maximum dose of 1 g daily.

The *BNFC* suggests the following doses:

- children aged 2 to 12 years; 5 mg/kg twice daily
- children aged 12 to 18 years; 250 mg twice daily for 2 weeks then adjusted to a maximum dose of 1 g daily

Doses are adjusted according to blood concentrations and response.

Preparations

USP 31: Cycloserine Capsules.

Proprietary Preparations (details are given in Part 3)

Austral.: Closina; ***Gr.:*** D-cycloserin; Seromycin; ***Hong Kong:*** Seromycin; ***India:*** Cyclorine; ***Thai.:*** Proserine; ***Turk.:*** Siklocap; ***UK:*** Cycloserine; ***USA:*** Seromycin.

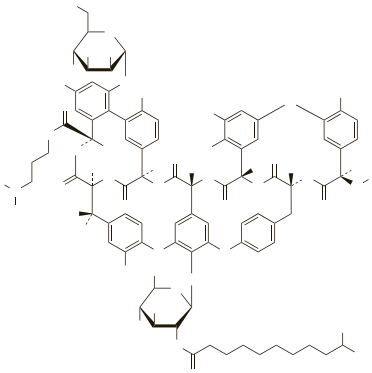
Dalbavancin *(BAN, USAN, rINN)*

A-A-1; BI-397; Dalbavancina; Dalbavancine; Dalbavancinum; MDL-63397; VER-001. 5,31-Dichloro-38-de(methoxycarbonyl)-7-demethyl-19-deoxy-56-*O*-{2-deoxy-2-[(10-methylundecanoyl)amino]-β-D-glucopyranuronosyl}-38-{[3-(dimethylamino)propyl]carbamoyl}-42-*O*-α-D-mannopyranosyl-15-*N*-methyl(ristomycin A aglicone) (main component).

Дальбаванцин

$C_{88}H_{100}Cl_2N_{10}O_{28}$ = 1816.7.

CAS — 171500-79-1.



Profile

Dalbavancin is a glycopeptide antibacterial under investigation for the treatment of severe infections due to Gram-positive bacteria, including complicated infections of the skin and soft tissues.

◊ References.

1. Lin S-W, *et al.* Dalbavancin: a new option for the treatment of gram-positive infections. *Ann Pharmacother* 2006; **40:** 449–60.
2. Billeter M, *et al.* Dalbavancin: a novel once-weekly lipoglycopeptide antibiotic. *Clin Infect Dis* 2008; **46:** 577–83.
3. Anderson VR, Keating GM. Dalbavancin. *Drugs* 2008; **68:** 639–48.
4. Bailey J, Summers KM. Dalbavancin: a new lipoglycopeptide antibiotic. *Am J Health-Syst Pharm* 2008; **65:** 599–610.

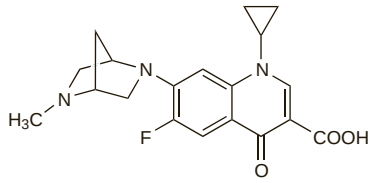
Danofloxacin Mesilate *(BANM, rINNM)*

CP-76136 (danofloxacin); CP-76136-27 (danofloxacin mesilate); Danofloksasiinimesilaatti; Danofloxacin Mesylate *(USAN)*; Danofloxacine, mésilate de; Danofloxacini mesilas; Danofloxacinmesilat; Mesilato de danofloxacino. 1-Cyclopropyl-6-fluoro-1,4-dihydro-7-[(1*S*,4*S*)-5-methyl-2,5-diazabicyclo[2.2.1]hept-2-yl]-4-oxo-3-quinolinecarboxylic acid monomethanesulphonate.

Данофлоксацина Мезилат

$C_{19}H_{20}FN_3O_3,CH_4O_3S$ = 453.5.

CAS — 112398-08-0 (danofloxacin); 119478-55-6 (danofloxacin mesilate).



(danofloxacin)

Profile

Danofloxacin is a fluoroquinolone antibacterial used as the mesilate in veterinary medicine for the treatment of susceptible infections in cattle and pigs.

Dapsone *(BAN, USAN, rINN)*

DADPS; Dapson; Dapsona; Dapsonas; Dapsoni; Dapsonum; Dapszon; DDS; Diaminodiphenylsulfone; Diaphenylsulfone; Disulone; NSC-6091; 4,4′-Sulfonylbis-benzenamine; Sulphonyldianiline. Bis(4-aminophenyl) sulphone.

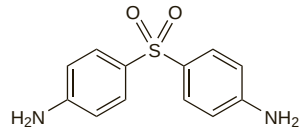
Дапсон

$C_{12}H_{12}N_2O_2S$ = 248.3.

CAS — 80-08-0.

ATC — J04BA02.

ATC Vet — QJ04BA02.



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

Ph. Eur. 6.2 (Dapsone). A white or slightly yellowish-white, crystalline powder. Very slightly soluble in water; sparingly soluble in alcohol; freely soluble in acetone. It dissolves freely in dilute mineral acids. Protect from light.

USP 31 (Dapsone). A white or creamy-white, odourless crystalline powder. Very slightly soluble in water, freely soluble in alcohol; soluble in acetone and in dilute mineral acids. Protect from light.

Stability. A study[1] of the stability of two extemporaneous oral suspensions of dapsone prepared from commercially available tablets found them to be stable for 3 months when stored at 4° and at 25°.

1. Nahata MC, *et al.* Stability of dapsone in two oral liquid dosage forms. *Ann Pharmacother* 2000; **34:** 848–50.

Adverse Effects

Varying degrees of dose-related haemolysis and methaemoglobinaemia are the most frequently reported adverse effects of dapsone, and occur in most patients given more than 200 mg daily; doses of up to 100 mg daily do not cause significant haemolysis, but patients with G6PD deficiency are affected by doses above about 50 mg daily.

Although agranulocytosis has been reported rarely with dapsone when used alone, reports have been more common when it has been used with other drugs in the prophylaxis of malaria. Deaths due to agranulocytosis, aplastic anaemia, and other blood dyscrasias have been reported.

Rash and pruritus may develop. Serious cutaneous hypersensitivity reactions occur rarely and include maculopapular rash, exfoliative dermatitis, toxic epidermal necrolysis, and Stevens-Johnson syndrome. Fixed drug eruptions have occurred.

A 'dapsone syndrome' may occur after 4 to 8 weeks of treatment and resembles mononucleosis in its presentation (see Hypersensitivity Reactions, below).

Peripheral neuropathy with motor loss has been reported in patients on dapsone for dermatological conditions. Peripheral neuropathy may occur as part of leprosy reaction states and is not an indication to stop dapsone.

Other adverse effects occur infrequently and include nausea, vomiting, anorexia, headache, hepatitis, insomnia, psychosis, and tachycardia.

Carcinogenicity. A survey of 1678 leprosy patients admitted for treatment to the National Hansen's Disease Center in the USA between 1939 and 1977 indicated that, although dapsone has been implicated as a carcinogen in *animals*, the use of dapsone did not appear to affect significantly the risk of cancer in these patients.[1] The International Agency for Research on Cancer concluded[2] that there was limited evidence for the carcinogenicity of dapsone in *animals* and insufficient data to be able to classify the carcinogenic risk in humans.

1. Brinton LA, *et al.* Cancer mortality among patients with Hansen's disease. *J Natl Cancer Inst* 1984; **72:** 109–14.
2. IARC/WHO. Some pharmaceutical drugs. *IARC monographs on the evaluation of carcinogenic risks to humans volume 24* 1980. Also available at: http://monographs.iarc.fr/ENG/Monographs/vol24/volume24.pdf Updated 07/04/88. (accessed 03/10/07)

Effects on the blood. *Haemolysis* is the most frequent serious adverse effect of dapsone and may occur at doses of 200 mg or higher daily.[1] Red blood cells may contain Heinz bodies and there is a reduction in their life span. Well-known risk factors include G6PD deficiency, methaemoglobin reductase deficiency, and haemoglobin M trait; haemoglobin E trait may also increase susceptibility to haemolytic reactions.[2] Haemolytic anaemia has been reported in a neonate after ingestion of dapsone in breast milk.[3]

Methaemoglobinaemia, although common, is rarely symptomatic.[1] However, severe cyanosis was associated with methaemoglobinaemia after an inadvertent overdose with dapsone in an HIV-positive patient with suspected pneumocystis pneumonia.[4] Methaemoglobinaemia has also been reported in an HIV-negative patient with severe renal impairment, who had previously undergone liver and kidney transplantations and who was receiving dapsone for prophylaxis of pneumocystis pneumonia.[5] The metabolite dapsone hydroxylamine is probably responsible for the methaemoglobinaemia and haemolysis associated with dapsone. Studies have shown[6,7] that use of dapsone with cimetidine, which inhibits production of the *N*-hydroxy metabolite, has resulted in a decrease in methaemoglobin levels, at least in the short term.

Agranulocytosis has occurred rarely on use of dapsone in leprosy and skin disease. More cases have been observed when used for malaria prophylaxis[8] (see also under Pyrimethamine, p.610) and dermatitis herpetiformis.[9] The reaction is usually self-limiting once the drug is withdrawn, but fatalities have occurred.[9,10]

Aplastic anaemia has been reported.[11,12] Of 11 fatalities attributed to dapsone reported to the British and Swedish adverse reaction registers[13] between 1968 and 1988, seven were due to white blood cell dyscrasias; none were attributed to red cell dyscrasias, although such reactions formed almost half of all serious reactions reported for dapsone.

Pure red cell aplasia has been reported in an elderly patient taking oral dapsone daily for granuloma annulare.[14]

Thrombocytosis was reported in a patient with AIDS receiving dapsone prophylactically.[15]

See also Hypoalbuminaemia, below.

1. Jopling WH. Side-effects of antileprosy drugs in common use. *Lepr Rev* 1983; **54:** 261–70.
2. Lachant NA, Tanaka KR. Case report: dapsone-associated Heinz body hemolytic anemia in a Cambodian woman with hemoglobin E trait. *Am J Med Sci* 1987; **294:** 364–8.
3. Sanders SW, *et al.* Hemolytic anemia induced by dapsone transmitted through breast milk. *Ann Intern Med* 1982; **96:** 465–6.
4. Seaton RA, *et al.* Blue and breathless. *Hosp Med* 1999; **60:** 530.
5. Ward KE, McCarthy MW. Dapsone-induced methemoglobinemia. *Ann Pharmacother* 1998; **32:** 549–53.
6. Coleman MD, *et al.* The use of cimetidine as a selective inhibitor of dapsone N-hydroxylation in man. *Br J Clin Pharmacol* 1990; **30:** 761–7.
7. Rhodes LE, *et al.* Cimetidine improves the therapeutic/toxic ratio of dapsone in patients on chronic dapsone therapy. *Br J Dermatol* 1995; **132:** 257–62.
8. Firkin FC, Mariani AF. Agranulocytosis due to dapsone. *Med J Aust* 1977; **2:** 247–51.
9. Cockburn EM, *et al.* Dapsone-induced agranulocytosis: spontaneous reporting data. *Br J Dermatol* 1993; **128:** 702–3.
10. Barss P. Fatal dapsone agranulocytosis in a Melanesian. *Lepr Rev* 1986; **57:** 63–6.
11. Foucauld J, *et al.* Dapsone and aplastic anemia. *Ann Intern Med* 1985; **102:** 139.
12. Meyerson MA, Cohen PR. Dapsone-induced aplastic anaemia in a woman with bullous systemic lupus erythematosus. *Mayo Clin Proc* 1994; **69:** 1159–62.
13. Björkman A, Phillips-Howard PA. Adverse reactions to sulfa drugs: implications for malaria chemotherapy. *Bull WHO* 1991; **69:** 297–304.
14. Borrás-Blasco J, *et al.* Pure red cell aplasia associated with dapsone therapy. *Ann Pharmacother* 2005; **39:** 1137–8.
15. Wynn RF, *et al.* Case report of dapsone-related thrombocytosis in an AIDS patient. *Am J Med* 1995; **98:** 602.

Effects on the eyes. There have been rare reports[1-4] of ocular toxicity, usually resulting in permanent loss of visual acuity, after overdoses with dapsone. Toxic effects included blurring of vision,[1,2] optic atrophy,[1] ischaemic retinopathy, ischaemic optic neuropathy,[3] and bilateral macular infarction.[4] These effects were thought to be due to acute hypoxia and obstruction with red cell fragments. A case of anterior ischaemic optic neuropathy[5] has also been reported in a patient taking usual doses of dapsone for dermatitis herpetiformis.

1. Daneshmend TK. The neurotoxicity of dapsone. *Adverse Drug React Acute Poisoning Rev* 1984; **3:** 43–58.
2. Alexander TA, *et al.* Presumed DDS ocular toxicity. *Indian J Ophthalmol* 1989; **37:** 150–1.