Florfenicol *(BAN, USAN, rINN)*

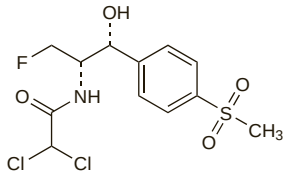
Florfénicol; Florfenicolum; Florfenikol; Florfenikoli; Sch-25298. 2,2-Dichloro-*N*-[(*αS*,*βR*)-α-(fluoromethyl)-β-hydroxy-4-methanesulfonylphenethyl]acetamide.

Флорфеникол

$C_{12}H_{14}Cl_2FNO_4S$ = 358.2.

CAS — 76639-94-6.

ATC Vet — QJ01BA90; QJ51BA90.



Profile

Florfenicol, a fluorinated analogue of chloramphenicol, is an antibacterial used in veterinary medicine.

Flucloxacillin *(BAN, rINN)*

BRL-2039; Floxacillin *(USAN)*; Flucloxacilina; Flucloxacilline; Flucloxacillinum; Flukloksasilin; Flukloksasilliini; Flukloxacillin. (6*R*)-6-[3-(2-Chloro-6-fluorophenyl)-5-methylisoxazole-4-carboxamido]penicillanic acid.

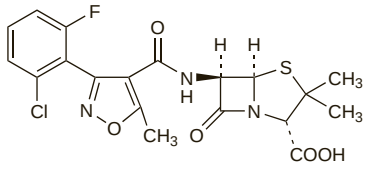
Флуклоксациллин

$C_{19}H_{17}ClFN_3O_5S$ = 453.9.

CAS — 5250-39-5.

ATC — J01CF05.

ATC Vet — QJ01CF05; QJ51CF05.



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

- Co-fluampicil (*BAN*)—flucloxacillin 1 part and ampicillin 1 part (w/w).

Flucloxacillin Magnesium *(BANM, rINNM)*

Flucloxacilina magnésica; Flucloxacilline Magnesique; Flucloxacilline-magnésium; Flucloxacillinum magnesicum; Magnesii Flucloxacillinum.

Магния Флуклоксациллин

$(C_{19}H_{16}ClFN_3O_5S)_2Mg,8H_2O$ = 1074.2.

CAS — 58486-36-5.

ATC — J01CF05.

ATC Vet — QJ01CF05.

Pharmacopoeias. In *Eur.* (see p.vii).

Ph. Eur. 6.2 (Flucloxacillin Magnesium Octahydrate). A white or almost white, crystalline powder. Slightly soluble in water; freely soluble in methyl alcohol. A 0.5% solution in water has a pH of 4.5 to 6.5.

Flucloxacillin Sodium *(BANM, rINNM)*

Flucloxacilina sódica; Flucloxacilline sodique; Flucloxacillinum natricum; Flucloxacillinum Natricum Monohydricum; Flukloksacilino natrio druska; Flukloksasilin Sodyum; Flukloksasilliininatrium; Flukloxacilin sodná sůl monohydrát; Flukloxacillinnatrium; Flukloxacillin-nátrium; Natrii Flucloxacillinum.

Натрий Флуклоксациллин

$C_{19}H_{16}ClFN_3NaO_5S,H_2O$ = 493.9.

CAS — 1847-24-1.

ATC — J01CF05.

ATC Vet — QJ01CF05.

Pharmacopoeias. In *Eur.* (see p.vii).

Ph. Eur. 6.2 (Flucloxacillin Sodium). A white or almost white, crystalline hygroscopic, powder. Freely soluble in water and in methyl alcohol; soluble in alcohol. A 10% solution in water has a pH of 5.0 to 7.0. Store at a temperature not exceeding 25° in airtight containers.

Incompatibility. As with other penicillins, flucloxacillin sodium is incompatible with aminoglycosides.

Adverse Effects and Precautions

As for Benzylpenicillin p.213.

Hepatitis and cholestatic jaundice have been reported occasionally with flucloxacillin and may be delayed in onset for up to 2 months after treatment has been stopped; older patients and those receiving flucloxacillin for more than 2 weeks are at greater risk. Fatalities have occurred, usually in patients with serious underlying hepatic disease. There have been rare reports of erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis associated with flucloxacillin. Agranulocytosis and neutropenia have been associated rarely with isoxazolyl penicillins such as flucloxacillin. Phlebitis has followed intravenous infusion.

Effects on the liver. In October 2004, the UK CSM issued a reminder[1] that flucloxacillin is associated rarely with an increased risk of hepatitis and cholestatic jaundice. In some patients, almost always those with serious underlying hepatic disease, fatalities have occurred. The onset of hepatic adverse effects may be delayed for up to 2 months after stopping treatment, and is not related to the dose or to the route. Older patients and those receiving flucloxacillin for more than 2 weeks are at increased risk. Flucloxacillin should not be used in patients with a history of hepatic dysfunction related to its use, and should be used only with caution in patients with evidence of other hepatic impairment. Careful enquiry should be made concerning previous hypersensitivity to beta lactams. A cohort study[2] using UK prescription data found that the risk of developing cholestatic liver disease in the 45 days after starting flucloxacillin was 8.5 per 100 000. In contrast to other countries, flucloxacillin continued to be seen as a first-line drug in the UK.

1. Committee on Safety of Medicines. Reminder: flucloxacillin and serious hepatic disorders. *Current Problems* 2004; **30:** 9. Available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON007448&RevisionSelectionMethod=LatestReleased (accessed 11/07/06)
2. Russmann S, *et al.* Risk of cholestatic liver disease associated with flucloxacillin and flucloxacillin prescribing habits in the UK: cohort study using data from the UK General Practice Research Database. *Br J Clin Pharmacol* 2005; **60:** 76–82.

Porphyria. Flucloxacillin has been associated with acute attacks of porphyria and is considered unsafe in porphyric patients.

Sodium content. Each g of flucloxacillin sodium contains about 2 mmol of sodium.

Interactions

As for Benzylpenicillin, p.214.

Antimicrobial Action

Flucloxacillin is bactericidal with a mode of action similar to that of benzylpenicillin, but is resistant to staphylococcal penicillinase. It is active therefore against penicillinase-producing and non-penicillinase-producing staphylococci. Its activity against streptococci such as *Streptococcus pneumoniae* and *Str. pyogenes* is less than that of benzylpenicillin, but sufficient to be useful when these organisms are present with penicillin-resistant staphylococci. Flucloxacillin is virtually ineffective against *Enterococcus faecalis*.

Resistance. The resistance of staphylococci to flucloxacillin and other penicillinase-resistant penicillins is described under meticillin (p.299).

Pharmacokinetics

Flucloxacillin is better absorbed from the gastrointestinal tract than cloxacillin, but absorption is reduced by the presence of food in the stomach. After an oral dose of 0.25 to 1 g, in fasting subjects, peak plasma concentrations in about 1 hour are usually in the range of 5 to 15 micrograms/mL. Plasma concentrations after intramuscular injection of flucloxacillin sodium are similar, but peak concentrations are achieved in about 30 minutes. Doubling the dose can double the plasma concentration. About 95% of flucloxacillin in the circulation is bound to plasma proteins. Flucloxacillin has been reported to have a plasma half-life of approximately 1 hour. The half-life is prolonged in neonates.

The distribution of flucloxacillin into body tissues and fluids is similar to that of cloxacillin (p.256).

Flucloxacillin is metabolised to a limited extent and the unchanged drug and metabolites are excreted in the urine by glomerular filtration and renal tubular secretion. About 66% of an oral dose and 76% of a parenteral dose is excreted in the urine within 8 hours. Only small amounts are excreted in the bile. Flucloxacillin is not removed by haemodialysis or peritoneal dialysis.

Plasma concentrations are enhanced by probenecid.

Uses and Administration

Flucloxacillin is an isoxazolyl penicillin used primarily for the treatment of infections due to staphylococci resistant to benzylpenicillin. These include bone and joint infections, endocarditis, pneumonia, skin infections (including soft-tissue infections), and toxic shock syndrome. For discussions of these infections and their treatment, see under Choice of Antibacterial, p.162.

Administration and dosage. Flucloxacillin is given parenterally and orally as the sodium or magnesium salt. All doses are expressed as flucloxacillin; 1.18 g of flucloxacillin magnesium and 1.09 g of flucloxacillin sodium are each equivalent to about 1 g of flucloxacillin. Oral doses should be taken at least 30 minutes before meals as the presence of food in the stomach reduces absorption. In severe renal impairment a reduction in dosage may be necessary.

The usual adult dose orally or by intramuscular injection is 250 mg four times daily. It is given intravenously in a dose of 0.25 to 1 g four times daily by slow injection over 3 to 4 minutes or by intravenous infusion. All systemic doses may be doubled in severe infections. Up to 8 g daily in 3 or 4 divided doses may be given for osteomyelitis; in endocarditis a dose of 8 g daily in 4 divided doses may be given to patients weighing up to 85 kg, and 12 g daily in 6 divided doses may be used in those weighing more.

Flucloxacillin has been given by other routes in conjunction with systemic therapy. It has been given in a dose of 250 to 500 mg daily by intra-articular injection, dissolved if necessary in a 0.5% solution of lidocaine hydrochloride, or by intrapleural injection in a dose of 250 mg daily. Using powder for injection, 125 to 250 mg has been dissolved in 3 mL of sterile water and inhaled by nebuliser 4 times daily.

Children up to 2 years of age may be given one-quarter the adult dose and those aged 2 to 10 years one-half the adult dose.

Flucloxacillin may be used with other antibacterials, including ampicillin (known as co-fluampicil), to produce a wider spectrum of activity. If flucloxacillin is given with an aminoglycoside the two drugs should not be mixed.

Preparations

BP 2008: Co-fluampicil Capsules; Co-fluampicil Oral Suspension; Flucloxacillin Capsules; Flucloxacillin Injection; Flucloxacillin Oral Solution; Flucloxacillin Oral Suspension.

Proprietary Preparations (details are given in Part 3)

Austral.: Flopen; Floxapen; Floxsig; Flubiclox; Flucil; Staphylex; ***Austria:*** Floxapen; ***Belg.:*** Floxapen; Staphycid; ***Chile:*** Fluxacina; Vitalpen; ***Denm.:*** Heracillin; ***Ger.:*** Fluclox; Flucloxa†; Staphylex; ***Hong Kong:*** Flucloxil; ***India:*** Floxapen†; ***Indon.:*** Floxapen; ***Irl.:*** Floxapen; Flucillin; Fluclon; Geriflox; ***Ital.:*** Betabiotic; Cloxillin; Evercid; Faifloc; Fareclox; Flucacid; Flucef; Flucinal; Fluclox; Fluxacil; Fluzerit; Liderclox; Nepenic; Pantaflux; Recaflux; ***Malaysia:*** Staphlex; ***Mex.:*** Floxapen; ***Neth.:*** Floxapen; Stafoxil†; ***NZ:*** Floxapen; Flucloxin; Staphlex; ***Philipp.:*** Stafloxin; ***Port.:*** Floxapen; Floxil†; ***S.Afr.:*** Floxapen; ***Singapore:*** Staphlex; ***Swed.:*** Heracillin; ***Switz.:*** Floxapen; ***Thai.:*** Staphycid; ***Turk.:*** Flix; Floksin; ***UK:*** Floxapen; Fluclomix; Ladropen; ***Venez.:*** Floxapen.

Multi-ingredient: ***Ger.:*** Flanamox; ***S.Afr.:*** Macropen; Megapen; Suprapen; ***UK:*** Magnapen.