

Flucloxacillin

Flucloxacillin as the sodium salt (Ph. Eur.) in 250 mg and 500 mg capsules, 250 mg/5 ml and 500 mg/5 ml powder for oral solution

Presentation

250 mg: Size '2' hard gelatine capsule having an opaque caramel body fitted with opaque grey cap. Both printed 'FXN 250' in black.

500 mg: Size "0E", hard gelatine, capsule having an opaque caramel body fitted with opaque grey cap. Both printed 'FXN 500' in black.

Oral Solution: Free flowing powder in 2 layers, the top layer being white, the bottom layer being pinkish. When reconstituted each 5 ml contains flucloxacillin sodium equivalent to 125 mg or 250 mg flucloxacillin.

Uses

Actions

Flucloxacillin sodium, a derivative of 6-amino-penicillanic acid, is a semi-synthetic penicillin with a narrow spectrum of bactericidal activity. Flucloxacillin, by its action on the synthesis of the bacterial wall, exerts a bactericidal effect on streptococci, staphylococci, including the beta-lactamase-producing strains, clostridia and neisseria. It is not active against methicillin-resistant staphylococci.

Strains of the following organisms are generally sensitive to the bactericidal action of flucloxacillin in vitro (the minimal inhibitory concentrations (MIC) of flucloxacillin are also quoted below).

Micro-organisms	MIC (mg/l)
Staphylococcus aureus	0.1 - 0.25
Staphylococcus aureus (beta- lactamase +)	0.25 - 0.5
Streptococcus pneumoniae	0.25
Streptococcus pyogenes (Group A beta-haemolytic)*	0.1
Streptococcus viridans group	0.5
Clostridium tetani	0.25
Clostridium welchii	0.25
Neisseria meningitidis	0.1
Neisseria gonorrhoeae	0.1
Neisseria gonorrhoeae (beta-lactamase +)	2.5

* The Group A beta-haemolytic streptococci are less sensitive to the isoxazolyl penicillins than to penicillin G or penicillin V.

Pharmacokinetic

Absorption: Flucloxacillin is stable in acid media and can therefore be administered either by the oral or parenteral route. The peak serum levels of flucloxacillin reached after 1 hour are as follows.

after 250 mg by the oral route (in fasting subjects): approximately 8.8 mg/l.
after 500 mg by the oral route (in fasting subjects): approximately 14.5 mg/l.

Absorption is more efficient when taken on an empty stomach. The total quantity absorbed by the oral route represents approximately 79% of the quantity administered.

Distribution: flucloxacillin diffuses well into most tissues. Specifically, active concentrations of flucloxacillin have been recovered in bones: 11.6 mg/l (compact bone) and 15.6 mg/l (spongy bone), with a mean serum level of 8.9 mg/l.

Crossing the meningeal barrier: flucloxacillin diffuses in only small proportion into the cerebrospinal fluid of subjects whose meninges are not inflamed.

Crossing into mother's milk: flucloxacillin is excreted in small quantities in mother's milk.

Metabolism: in normal subjects approximately 10% of the flucloxacillin administered is metabolized to penicilloic acid. The elimination half-life of flucloxacillin is 30-60 minutes.

Excretion: the drug is rapidly excreted by the kidney, about 50% within 6 hours of administration. A small portion of the dose administered is excreted in the bile. The excretion of flucloxacillin is slowed in cases of renal failure.

Protein Binding: the serum protein binding rate is 95 %.

Indications

FLUCLOXACILLIN is indicated for the treatment of infections due to Gram-positive organisms, including infections caused by β -lactamase producing staphylococci.

Typical indications include:

Skin and Soft Tissue Infections: Boils, abscesses, carbuncles, furunculosis, cellulitis, infected wounds, infected burns, protection of skin grafts, and impetigo.

Infected Skin Conditions: ulcer, eczema and acne.

Respiratory Tract Infections: Pneumonia, lung abscess, empyema, sinusitis, pharyngitis, tonsillitis, quinsy, otitis media and externa.

Other infections caused by flucloxacillin-sensitive organisms such as osteomyelitis, enteritis, endocarditis, urinary tract infection, meningitis, septicaemia.

Oral preparations of the β -lactamase-resistant penicillins (or flucloxacillin) should not be used as initial therapy in serious, life threatening infections. Oral therapy with flucloxacillin may be used to follow up the previous use of parenteral flucloxacillin as soon as the clinical condition warrants.

Dosage and administration

Adults (including elderly patients): 500 mg initially and then either 500 mg or 250 mg 8-hourly depending on severity of infection.

Children 2-10 years: 250 mg initially, then 125 mg 8-hourly.

Children under 2 years: Half the recommended dose for children 2-10 years

Doses should be administered 1 hour before meals.

Contraindications

Flucloxacillin is a penicillin and should not be given to patients with a history of hypersensitivity to beta-lactam antibiotics (eg. penicillins, cephalosporins) or excipients.

Flucloxacillin is contraindicated in patients with a previous history of flucloxacillin-associated jaundice/hepatic dysfunction.

Warnings and Precautions

Before initiating therapy with flucloxacillin, careful inquiry should be made concerning previous hypersensitivity reactions to beta-lactams. Cross-sensitivity between penicillins and cephalosporins is well documented.

Serious and occasionally fatal hypersensitivity reactions (anaphylaxis) have been reported in patients receiving beta-lactam antibiotics. Although anaphylaxis is more frequent following parenteral therapy, it has occurred in patients on oral therapy. These reactions are more likely to occur in individuals with a history of beta-lactam hypersensitivity. If an allergic reaction occurs, flucloxacillin should be discontinued and the appropriate therapy instituted. Serious anaphylactoid reactions may require immediate emergency treatment with adrenaline. Oxygen, intravenous steroids, and airway management, including intubation, may also be required.

Hepatitis, predominantly of a cholestatic type has been reported and, very rarely, deaths have occurred, almost always in patients with serious underlying disease. Reports have been more frequent with increasing age or following prolonged treatment (*see Adverse Effects*). Flucloxacillin should be used with caution in patients with evidence of hepatic dysfunction.

Special caution is essential in the newborn because of the risk of hyperbilirubinemia. Studies have shown that, at high dose following parenteral administration, flucloxacillin can displace bilirubin from plasma protein binding sites, and may therefore predispose to kernicterus in a jaundiced baby. In addition, special caution is essential in the newborn because of the potential for high serum levels of flucloxacillin due to a reduced rate of renal excretion.

During prolonged treatments (eg osteomyelitis, endocarditis), regular monitoring of hepatic and renal functions is recommended.

Prolonged use may occasionally result in overgrowth of non-susceptible organisms.

Dosage should be adjusted in renal impairment. (*see Dosage and Administration*)

FLUCLOXACILLIN Oral Solution contains sodium benzoate (5 mg/5 ml).

Use in pregnancy: (Category B1) Penicillins are generally considered safe for use in pregnancy. Animal studies with flucloxacillin have shown no teratogenic effects. Limited information is available concerning the results of the use of flucloxacillin in human pregnancy. Flucloxacillin should only be used in pregnancy when the potential benefits outweigh the potential risks associated with treatment.

Use during lactation: Trace quantities of flucloxacillin are excreted in breast milk. Flucloxacillin may be administered during the period of lactation. With the exception of the risk of sensitization, there are no detrimental effects for the breastfed infant.

Effects on ability to drive and use machines: adverse effects on the ability to drive or operate machinery have not been observed.

Adverse Effects

Hypersensitivity reactions: if any hypersensitivity reaction occurs, the treatment should be discontinued.

Rash, urticaria, purpura, fever, eosinophilia; sometimes angioneurotic oedema, rarely anaphylactic shock (exceptional with oral administration) (*see Warnings and Precautions*). Certain reactions (fever, arthralgia, myalgia) sometimes develop more than 48 hours after the start of the treatment. Erythema multiforme has been reported rarely.

Gastrointestinal reactions: minor gastrointestinal disturbances may occur during treatment. As with other antibiotics, pseudomembranous colitis has been reported rarely. If this condition develops, flucloxacillin treatment should be discontinued and appropriate therapy, e.g. oral vancomycin should be initiated.

Hepatic effects: hepatitis and cholestatic jaundice have been reported (*see Warnings and Precautions*). These may be delayed for up to two months post-treatment. In some cases the course has been protracted and lasted for several months. Very rarely, deaths have been reported, almost always in patients with serious underlying disease.

Changes in liver function test results may occur, but are reversible when treatment is discontinued.

Renal effects: interstitial nephritis may occur but is reversible when treatment is discontinued.
Haematological effects:

Neutropenia (including agranulocytosis) and thrombocytopenia may occur but are reversible when treatment is discontinued.

Neurological Effects: In patients suffering from renal failure, neurological disorders with convulsions are possible with high doses (mainly parenteral).

Interactions

Bacteriostatic agents may interfere with the bactericidal action of flucloxacillin.

Probenicid decreases the renal tubular secretion of flucloxacillin. Concurrent administration of probenicid delays the renal excretion of flucloxacillin.

Chloramphenicol, Erythromycin, Sulfonamides or Tetracyclines: Since bacteriostatic agents may interfere with the bactericidal effect of penicillins in the treatment of meningitis or other situations where a rapid bactericidal effect is necessary, it is best to avoid concurrent therapy.

Contraceptives: Flucloxacillin may decrease the efficacy of oestrogen-containing oral contraceptives.

Aminoglycosides: if flucloxacillin is to be used concurrently with an aminoglycoside, the two antibiotics should not be mixed.

Doses should be administered 1 hour before meals.

Overdosage

Gastrointestinal effects such as nausea, vomiting and diarrhoea may be evident and should be treated symptomatically. Flucloxacillin is not removed from the circulation by haemodialysis.

Pharmaceutical Precautions

Capsules: Store below 25 °C.

Oral solutions: Store below 25 °C.

Shelf-life:

Capsules: packed in bottles: 36 months stored at or below 25 °C. Protect from light

Capsules packed in blisters: 24 months stored at or below 25 °C. Protect from light

Powder for Oral Solution: 24 months stored below 25 °C. Once reconstituted 14 days at 2-8 °C. Protect from light

Medicine Classification

Prescription Only Medicine.

Package Quantities

Capsules: 250 mg: 250's in bottles and 20s in blisters.

500 mg: 250's and 500's in bottles and 20s in blisters.

Powder for Oral Solution: 100 ml bottles.

Further Information

Flucloxacillin is (6R)-6-[3-(2-chloro-6-fluorophenyl)-5-methyl-isoxazole-4-carboxamido] penicillanic acid. It has the chemical formula $C_{19}H_{17}ClFN_3O_5S$ and a molecular weight of 453.88.

Other ingredients of the capsules are: magnesium stearate and silicon dioxide.

Other ingredients of the oral solution are: sodium benzoate, disodium edetate, saccharin sodium, sodium citrate, ammonium glycyrrhizinate, sucrose, FD&C Red, pineapple flavour and menthol flavour.

Name and Address

AFT Pharmaceuticals Ltd
PO Box 33-203
Auckland
Telephone: (09) 488-0232

Date of Preparation

19 April 2006