

DATA SHEET

FLUCLOXIN

Flucloxacillin as the sodium salt in 250 mg, 500 mg and 1 g injections.

Presentation

Flucloxacillin as the sodium salt in:

250 mg injection: Type III glass vials containing a white powder for reconstitution and labelled with the appropriate content of flucloxacillin.

500 mg injection: Type III glass vials containing a white powder for reconstitution and labelled with the appropriate content of flucloxacillin.

1 g injection: Type III glass vials containing a white powder for reconstitution and labelled with the appropriate content of flucloxacillin.

Uses

Actions

Flucloxacillin sodium, a derivative of 6-amino-penicillanic acid, is a semi-synthetic penicillin with a narrow spectrum of bactericidal activity directed primarily against gram positive bacteria. Its mechanism of action is similar to that of benzyl penicillin in that it inhibits formation of the cell wall in susceptible species. Flucloxacillin is resistant to hydrolysis by acid and penicillinase.

Pharmacokinetics

Flucloxacillin is well absorbed after either oral or intramuscular administration. Peak serum concentrations after intramuscular administration of 250 mg-1 g may range from 5-15 μ g/mL after 30 minutes. Therapeutic concentrations persist for about 4 hours.

Once absorbed, about 95% of flucloxacillin in the circulation is bound to plasma protein. Flucloxacillin is metabolised to a limited extent and the unchanged drug and metabolites are excreted by the kidneys by both tubular secretion and glomerular filtration. Approximately 90% of an intramuscular dose is excreted in the urine within 6 hours. The elimination half-life has been measured as 1.31-1.39 hours. The half-life is extended in neonates.

Elimination of flucloxacillin is decreased in renal failure and in the elderly, but dosage adjustment is only required if creatinine clearance is less than 10 mL/min.

Indications

FLUCLOXIN is indicated for the treatment of skin and soft tissue infections caused by susceptible organisms and infections due to penicillinase producing staphylococci and for mixed streptococcal and staphylococcal infections where the staphylococci are resistant to penicillin. For example, infections of the joints, respiratory tract and urinary tract, otitis media, endocarditis, septicaemia, and meningitis.

FLUCLOXIN is also used in the prophylaxis of staphylococcal infections during major surgical procedures, particularly in cardiothoracic or orthopaedic surgery.

Dosage and Administration

FLUCLOXIN is to be administered by injection.

Adults

Intramuscular: Dissolve 250 mg vial content in 1.5 ml water for injection, 500 mg vial content in 2 ml water for injection, 1 g vial content in 2.5 ml water for injection. Usual adult dosage 250 mg every 6 hours.

Intravenous: Dissolve 250 mg to 500 mg in 10 ml or 1 g in 15 ml to 20 ml of water for injection and administer by slow intravenous injection (3 to 4 minutes).

FLUCLOXIN may also be added to infusion fluids or injected, suitably diluted, into the drip tube over a period of 3 to 4 minutes. Usual adult dosage 250 mg to 1 g every 6 hours.

Intrapleural: Dissolve 250 mg in 5 to 10 ml water for injection. Usual adult dosage 250 mg once daily.

Intraarticular: Dissolve 250 mg to 500 mg in up to 5 ml water for injection or in 0.5% lignocaine hydrochloride solution. Usual adult dose 250 mg to 500 mg once daily.

Children

Up to 2 years of age: One quarter of the adult dose.

2 years to 10 years: Half the adult dose.

Children have been given doses of 12.5 mg/kg body weight four times a day.

FLUCLOXIN may be used in combination with other antibiotics, particularly ampicillin, to produce a wider spectrum of activity. If used concurrently with aminoglycosides, the two antibiotics should not be mixed.

Contraindications

The use of this agent is contraindicated in individuals with a history of an allergic reaction to the penicillins and in patients with a previous history of flucloxacillin-associated jaundice/hepatic dysfunction.

Warnings and Precautions

Serious and occasionally fatal hypersensitivity (anaphylactoid) reactions have been reported in patients on penicillin therapy. Although anaphylaxis is more frequent following parenteral therapy, it has occurred in patients on oral penicillins.

Before commencing therapy with any penicillin, careful enquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins or other allergens. If an allergic reaction occurs; appropriate therapy should be instituted and **FLUCLOXIN** therapy discontinued.

Serious anaphylactoid reactions require emergency treatment with adrenalin, oxygen and intravenous steroids. Airway management including intubation should also be administered as indicated.

As with any potent medicine, periodic assessment of renal, hepatic and haematopoietic function should be made during prolonged therapy. The possibility of superinfections with mycotic or bacterial pathogens should be kept in mind during therapy. If superinfections occur (usually involving *Aerobacter*, *Pseudomonas* or *Candida*), the medicine should be discontinued and/or appropriate therapy instituted.

Hepatitis, predominantly of the cholestatic type has been reported to be associated with flucloxacillin therapy. Reports have been more frequent with increasing age or following prolonged treatment. Jaundice may first appear several weeks after therapy. Although resolution has occurred with time in most cases, hepatic dysfunction may be prolonged. Some patients have died of hepatitis associated with flucloxacillin.

Pseudomembranous colitis due to *Clostridium difficile* has been reported with virtually all broad-spectrum antibiotics, therefore, it is important to consider its diagnosis in patients who develop diarrhoea in association with the use of flucloxacillin. Such colitis may range in severity from mild to life-threatening. Mild cases of pseudomembranous colitis usually respond to medicine discontinuance alone. In moderate to severe cases appropriate measures should be taken. Diarrhoea may also occur after the cessation of therapy.

The use of flucloxacillin could potentially result in the reduction of albumin-bound bilirubin. Flucloxacillin should, therefore, be used with caution in neonates and premature infants because of the risk of hyperbilirubinaemia.

Use in Pregnancy: Safety for use of flucloxacillin in the first trimester of pregnancy has not been established. Use in the second and third trimester of pregnancy, and when breast feeding, has shown no significant risk to the neonate. Studies in animals have not shown evidence of fetal damage.

FLUCLOXIN does, however, cross the placental barrier and is excreted in breast milk, so there may be a possibility of sensitisation, diarrhoea, candidiasis and skin rash in the infant.

Adverse Effects

As with other penicillins, it may be expected that untoward reactions will be essentially limited to sensitivity phenomena.

They are more likely to occur in individuals who have previously demonstrated hypersensitivity to penicillins. The following adverse reactions have been reported as associated with the use of flucloxacillin.

Gastrointestinal: Nausea, vomiting, diarrhoea.

Hypersensitivity Reactions: Erythematous maculopapular rashes, urticaria or wheezing. Whenever such reactions occur, **FLUCLOXIN** should be discontinued (note: urticaria, other skin rashes and serum sickness-like reactions may be controlled with antihistamines and, if necessary, systemic corticosteroids).

Liver: A moderate rise in SGOT and cholestasis have been reported. Hepatitis and cholestatic jaundice (sometimes severe) have been reported with a frequency of approximately 1.15000 exposures.

Haemic and Lymphatic Systems: Such reactions as anaemia, thrombocytopenia, thrombocytopenic purpura, eosinophilia, leucopenia and agranulocytosis have been reported during therapy with other penicillins. These reactions are usually reversible on discontinuation of therapy and are believed to be hypersensitivity phenomena.

Interactions

Flucloxacillin should not be mixed with blood products or other proteinaceous fluids.

Probenecid decreases renal tubular secretion of penicillins when used concurrently, resulting in increased and more prolonged flucloxacillin serum concentrations and prolonged elimination half-life.

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.

Overdosage

No incidence of overdosage has been reported.

Pharmaceutical Precautions

Injections: Store the unprepared powder in a cool, dry place protected from light. The injections should be prepared immediately before use and any unused solution discarded. Once prepared the injections need to be checked for absence of particulate matter before use.

Medicine Classification

Prescription Medicine.

Package Quantities

250mg, 500mg and 1 g Injections: 5 vials

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.

1.09 g of flucloxacillin sodium is approximately equivalent to 1 g of anhydrous flucloxacillin.

Flucloxacillin injection is compatible with the following infusion fluids for a period not exceeding 1 hour at room temperature: Dextrose 5%, Dextrose/Saline, Hartman's Ringers, 0.9% sodium chloride, dextrans.

Flucloxacillin injection is stable when reconstituted in water for injection for at least 72 hours when stored at 5°C. It is compatible with the following infusion fluids for up to 72 hours when stored at 5°C: Dextrose 5%, 0.9% sodium chloride and dextrose/saline.

Since the dry powder in a vial displaces a set volume once it is in solution, this must be allowed for by calculating the volume of diluent to be added to ensure the correct dose is given.

250 mg of stated activity displaces 0.2 mL of diluent.

500 mg of stated activity displaces 0.4 mL of diluent.

1000 mg of stated activity displaces 0.8 mL of diluent.

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