

Data Sheet

STAPHLEX

Flucloxacillin (as the sodium salt) 250 mg and 500 mg capsules, and 125mg/5ml and 250mg/5ml powder for syrup

Presentation

Flucloxacillin Capsule 250mg: Yellow body, Black Cap, Size 2, contains a white powder. Each capsule contains 250mg flucloxacillin (as the sodium salt).

Flucloxacillin Capsule 500mg: Yellow body, Black Cap, Size 0, contains a white powder. Each capsule contains 500mg flucloxacillin (as the sodium salt).

Flucloxacillin Syrup 125mg/5mL: White to off white free-flowing powder with an odour of orange. When reconstituted it readily produces an orange coloured completely homogenous solution. Each 5mL of reconstituted solution contains 125mg flucloxacillin (as the sodium salt).

Flucloxacillin Syrup 250mg/5mL: White to off white free-flowing powder with an odour of orange. When reconstituted it readily produces an orange coloured completely homogenous solution. Each 5mL of reconstituted solution contains 250mg flucloxacillin (as the sodium salt).

Uses

Flucloxacillin is an isoxazolyl penicillin of the beta-lactam group of antibiotics, which exerts a bactericidal effect upon many Gram positive organisms including streptococci and beta-lactamase producing staphylococci.

Actions

Properties:

Flucloxacillin is a narrow-spectrum antibiotic of the group of isoxazolylpenicillins; it is not inactivated by staphylococcal beta-lactamases.

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 quoted below.)

Micro-organisms	MIC (mg/L)
<i>Staphylococcus aureus</i>	0.1 - 0.25
<i>Staphylococcus aureus</i> (beta- lactamase +)	0.25 - 0.5
<i>Streptococcus pneumoniae</i>	0.25
<i>Streptococcus pyogenes</i> (Group A beta-haemolytic)*	0.1
<i>Streptococcus viridans</i> group	0.5
<i>Clostridium tetani</i>	0.25
<i>Clostridium welchii</i>	0.25

<i>Neisseria meningitidis</i>	0.1
<i>Neisseria gonorrhoeae</i>	0.1
<i>Neisseria gonorrhoeae</i> (beta-lactamase +)	2.5

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

Pharmacokinetics

Absorption:

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

- After 250mg by the oral route (in fasting subjects): approximately 8.8 mg/L.
- After 500mg by the oral route (in fasting subjects): approximately 14.5 mg/L.

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 of the order of 53 minutes.

Excretion:

Excretion occurs mainly through the kidney. Between 65.5% (oral route) and 76.1% (parenteral route) of the dose administered is recovered in unaltered active form in the urine within 8 hours. 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%.

Preclinical Safety Data

No further information of relevance to add.

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:

e.g. 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):

500mg initially and then either 500mg or 250mg 8-hourly depending on severity of infection.

Children 2-10 years:

250mg initially, then 125mg 8-hourly.

Children Under 2 Years:

Half this dose.

Oral doses should be administered 1 hour before meals.

Renal Impairment

The excretion of flucloxacillin is slowed in cases of renal failure. If creatinine clearance drops below 10mL/min, then the recommended dosage is 1g every 8 to 12 hours. (In anuric patients, the maximum dosage is 1g every 12 hours).

Neither haemodialysis nor peritoneal dialysis lower the serum levels of flucloxacillin. Therefore, dialysis need not be accompanied by an additional dose.

Contraindications

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

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

Ocular administration.

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 (anaphylactoid) reactions 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.

Flucloxacillin should be used with caution in patients with evidence of hepatic dysfunction, those with serious underlying disease, and the elderly. In these patients, hepatic events may be severe, and in extremely rare circumstances, deaths have been reported (see Adverse Effects).

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 (e.g. osteomyelitis, endocarditis), regular monitoring of hepatic and renal functions is recommended.

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

Sodium content:

Each 1 gram of flucloxacillin sodium contains 2.2 mmol of sodium. This should be included in the daily allowance of patients on sodium restricted diets.

Magnesium content:

Each 1 gram of flucloxacillin magnesium contains approximately 1 mmol of magnesium. This should be considered for patients with impaired renal function (creatinine clearance of less than 30mL/min).

Dosage should be adjusted in renal impairment.

Pregnancy and lactation

Pregnancy:

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.

Lactation:

Flucloxacillin is excreted in breast milk in trace amounts.

Flucloxacillin may be administered during the period of lactation. With the exception of the risk of sensitisation, 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

The following convention has been utilised for the classification of undesirable effects:- Very common (>1/10), common (>1/100, <1/10), uncommon (>1/1000, <1/100), rare (>1/10,000, <1/1000), very rare (<1/10,000).

Unless otherwise stated, the frequency of the adverse events has been derived from more than 30 years of post-marketing reports.

Musculoskeletal and connective tissue disorders:

Very rare: Arthralgia and myalgia sometimes develop more than 48 hours after the start of the treatment.

Gastrointestinal disorders:

Clinical trial data

*Common: Minor gastrointestinal disturbances.

Post marketing Data

Very rare: Pseudomembranous colitis.

If Pseudomembranous colitis develops, flucloxacillin treatment should be discontinued and appropriate therapy, e.g. oral vancomycin should be initiated.

Immune system disorders:

Very rare: anaphylactic shock (exceptional with oral administration) (see Warnings), angioneurotic oedema.

If any hypersensitivity reactions occur, flucloxacillin should be discontinued. (See also Skin and subcutaneous tissue disorders).

Renal and Urinary disorders:

Very rare: Interstitial nephritis.

This is reversible when treatment is discontinued.

Hepato-biliary disorders:

Very rare: Hepatitis and cholestatic jaundice (See Warnings and Precautions). Changes in liver function laboratory test results (reversible when treatment is discontinued).

Hepatitis and cholestatic jaundice 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.

Skin and subcutaneous tissue disorders:

Clinical Trial Data

*Uncommon: Rash, urticaria and purpura.

Post Marketing Data

Very rare: Erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis.

(See also Immune system disorders).

Nervous system disorders:

Very rare: In patients suffering from renal failure, neurological disorders with convulsions are possible with the I.V. injection of high doses.

Blood and lymphatic system disorders:

Very rare: neutropenia (including agranulocytosis) and thrombocytopenia. These are reversible when treatment is discontinued. Eosinophilia. Haemolytic anaemia.

*The incidence of these AEs was derived from clinical studies involving a total of approximately 929 adult and paediatric patients taking flucloxacillin.

Interactions

Probenecid decreases the renal tubular secretion of flucloxacillin. Concurrent administration of probenecid delays the excretion of flucloxacillin.

Bacteriostatic agents may interfere with the bactericidal action of flucloxacillin.

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.

Syrups: Store below 25°C. Once dispensed, Flucloxacillin Syrups remain stable for fourteen days if stored under refrigeration (2°C to 8°C).

Medicine Classification

Prescription Medicine.

Package Quantities

STAPHLEX Syrup: Not marketed

STAPHLEX 250 mg capsules: Bottles of 100's, 500's and 250's.

STAPHLEX 500 mg capsules: Bottles of 50's, 250's and 500's.

Not all pack sizes may be marketed.

Further Information

Nil.

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