

1. NAME OF THE MEDICINAL PRODUCT

FLUXALIN 500 mg Injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial contains:

Flucloxacillin Sodium Monohydrate BP

Equivalent to Flucloxacillin 500 mg

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Powder for Injection

A white or almost white, hygroscopic crystalline powder

4. CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Flucloxacillin is indicated for the treatment of infections due to penicillinase producing staphylococci and other gram positive organisms susceptible to this anti-infective. Indications include: osteomyelitis and endocarditis.

Flucloxacillin is also indicated for use as a prophylactic agent during major surgical procedures when appropriate; for example cardiothoracic and orthopedic surgery. Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 DOSAGE AND ADMINISTRATION

The dosage depends on the severity and nature of the infection.

The usual routes of administration are by intramuscular injection, slow intravenous injection and intravenous infusion.. The solutions must be prepared as follows:

Intramuscular: 2ml of water for injections to 500mg vial contents.

Intravenous: Dissolve 500mg in 5 to 10ml of water for injections. Administer by slow intravenous injection (over three to four minutes). Flucloxacillin may also be added to infusion fluids or injected (suitably diluted) into the drip tube over three to four minutes. Flucloxacillin may be added to most intravenous fluids (eg water for injections, sodium chloride 0.9%, glucose 5%, sodium chloride 0.18% with glucose 4%).

Children

Any route of administration may be used. For children under two years old, a quarter of the adult dose should be administered. For children two to ten years old, half of the adult dose should be administered.

Impaired renal function:

Dosage reduction is not usually required. In severe renal failure, however, (creatinine clearance less than 10ml/min) a reduction in dose or extension of dose interval should be considered.

No supplementary dosages need be administered during or at the end of the dialysis period, as flucloxacillin is not significantly removed by dialysis.

4.3 CONTRAINDICATIONS

Flucloxacillin should not be given to patients with a history of hypersensitivity to β -lactam antibiotics (e.g. penicillins, cephalosporins). Flucloxacillin is contraindicated in patients with a previous history of Flucloxacillin-associated jaundice/hepatic dysfunction.

Ocular or subconjunctival administration is contraindicated.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE WARNINGS

Flucloxacillin should be given with caution to patients with a history of allergy, especially to drugs. Before initiating therapy with Flucloxacillin, careful enquiry should be made concerning previous hypersensitivity reactions to β -lactams. Cross sensitivity between penicillins and cephalosporins is well documented. Serious and occasionally fatal hypersensitivity reactions (anaphylaxis) have been reported in patients receiving β -lactam antibiotics. These reactions are more likely to occur in individuals with a history of β -lactam hypersensitivity. Desensitization may be necessary if treatment is essential. If any hypersensitivity reaction occurs, the treatment should be discontinued.

Care is necessary if very high doses of Flucloxacillin are given, especially if renal function is poor, because of the risk of nephrotoxicity and/or neurotoxicity. The intrathecal route should be avoided. Care is also necessary if large doses of sodium salts are given to patients with impaired renal function or heart failure. Flucloxacillin should be used with caution in patients with evidence of hepatic dysfunction (see section 4.8). Renal, hepatic and haematological status should be monitored during prolonged and highdose therapy (e.g.

osteomyelitis, endocarditis). Prolonged use may occasionally result in overgrowth of non-susceptible organisms.

Care is required when treating some patients with spirochete infections such as syphilis or leptospirosis because the Jarisch- Herxheimer reaction may occur shortly after treatment with a penicillin is started.

In case of severe and persistent diarrhoea, the possibility of pseudomembranous colitis should be considered; Flucloxacillin therapy should be discontinued.

Contact with Flucloxacillin should be avoided since skin sensitisation may occur.

Caution is advised in patients with porphyria.

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.

Sodium content: Flucloxacillin for Injection 500mg contains approximately 1.13mmol sodium per vial. This should be included in the daily allowance of patients on sodium restricted diets.

4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

Other Antibacterials: Since bacteriostatic drugs such as chloramphenicol and tetracycline may interfere with the bactericidal effect of penicillins in the treatment of meningitis or in other situations in which a rapid bactericidal effect is necessary, it is best to avoid concurrent therapy.

Immunosuppressant: There is reduced excretion of methotrexate (increased risk of toxicity).

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

Uricosuric agents: Plasma concentrations of Flucloxacillin are enhanced if probenecid is given concurrently.

Interference with diagnostic tests: Penicillins may produce false-positive results with the direct antiglobulin (Coombs') test, falsely high urinary glucose results with the copper sulphate test and falsely high urinary protein results, but glucose enzymatic tests (e.g.

Clinistix) and bromophenol blue tests (e.g. Multistix or Albustix) are not affected.

4.6 PREGNANCY AND LACTATION

There has been no evidence of a teratogenic effect in animals or untoward effect in humans. However, use in pregnancy should be reserved for essential cases.

Trace quantities of penicillin can be detected in breast milk with the potential for hypersensitivity reactions (e.g. drug rashes) in the breast-fed neonate or acute alterations in the neonatal bowel flora with resultant diarrhoea.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

None.

4.8 UNDESIRABLE EFFECTS

Blood and lymphatic system disorders: Transient leucopenia, thrombocytopenia, haemolytic anaemia, agranulocytosis and neutropenia (which might have some immunological basis); prolongation of bleeding time and defective platelet function are generally associated with large intravenous doses of Flucloxacillin or impaired renal function.

Immune system disorders: The most common adverse effects are sensitivity reactions including urticaria, maculo-papular rashes, pruritus, fever, joint pains and angioedema.

Anaphylaxis occasionally occurs and has sometimes been fatal. Late sensitivity reactions may include serum sickness-like reactions (featuring symptoms such as arthralgia, rash, urticaria, fever, angioedema, lymphadenopathy), haemolytic anaemia, nephropathy and acute interstitial nephritis, which is reversible when treatment is discontinued.

Some patients with spirochaete infections such as syphilis or leptospirosis may experience a Jarisch-Herxheimer reaction shortly after treatment with a penicillin is started. Symptoms include fever, chills, headache and reaction at the site of lesions. The reaction can be dangerous in cardiovascular syphilis or where there is a serious risk of increased local damage such as with optic atrophy.

Metabolism and nutrition disorders: Electrolyte disturbances, such as hypokalaemia, due to administration of large amounts of sodium, are generally associated with large intravenous doses of Flucloxacillin or impaired renal function.

Psychiatric disorders: Hallucinations.

Nervous system disorders: Convulsions and other signs of central nervous system toxicity are generally associated with large intravenous doses of Flucloxacillin or impaired renal function. Encephalopathy has been reported following intrathecal administration and can be fatal. Coma may develop with high doses of Flucloxacillin. Respiratory, thoracic and mediastinal disorders: Acute, severe dyspnoea; bronchospasm. **Gastrointestinal disorders:** Diarrhoea, nausea and vomiting, reported with Flucloxacillin, commonly occur after oral or parenteral administration. Pseudomembranous colitis has been reported with most antibiotics. Prolonged use of penicillins may lead to the development of oral candidiasis.

Hepatobiliary disorders: Changes in liver function test results may occur, but are reversible when treatment is discontinued. Hepatitis and cholestatic jaundice have been reported. These reactions are related neither to the dose nor to the route of administration; administration for more than two weeks and increasing age are risk factors. The onset of these effects may be delayed for up to two months post-treatment; in several cases the course of the reactions has been protracted and lasted for some months. In very rare cases, a fatal outcome has been reported, almost always in patients with serious underlying disease.

Skin and subcutaneous tissue disorders: Erythema multiforme; Stevens-Johnson syndrome; toxic epidermal necrolysis (Lyell's syndrome); erythema nodosum; pemphigoid reactions; non-thrombocytopenic purpura; vasculitis. **Congenital, familial and genetic disorders:** Acute attacks of porphyria

General disorders and administration site conditions: Phlebitis has followed intravenous infusion.

4.9 OVERDOSE

Symptoms

With high parenteral doses of penicillins, neurotoxicity (e.g. convulsions, encephalopathy), blood disorders (e.g. neutropenia, haemolytic anaemia, prolongation of bleeding time, defective platelet function) or electrolyte disturbances may occur.

Treatment

Treatment is symptomatic. Flucloxacillin is not removed from the circulation by haemodialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMICS PROPERTIES

Pharmacotherapeutic group: Antibacterials for systemic use, Beta-lactamase resistant penicillins

ATC code: J01CF05.

Flucloxacillin is bactericidal with a similar mode of action to benzylpenicillin. It is resistant to staphylococcal penicillinase and therefore active against penicillinase-producing and non-penicillinase-producing staphylococci. It has minimum inhibitory concentrations in the range of 0.25 to 0.5 µg per ml. 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. It is virtually ineffective against *Enterococcus faecalis*.

5.2 PHARMACOKINETIC PROPERTIES

After the intramuscular administration of a single 250 or 500mg dose of flucloxacillin to volunteers, mean peak concentrations of the drug in serum were approximately 10.5 and 16 mg.l⁻¹ respectively. Mean urinary excretion of Flucloxacillin following its intramuscular use is 61% of the administered dose.

Flucloxacillin may also be administered by intravenous bolus injection or by slow intravenous infusion. High serum levels of the drug are achieved by these modes of administration: 30 minutes and 2 hours after a single 500mg intravenous bolus injection of Flucloxacillin the mean serum concentration of the drug was 38 and 7.5 mg.l⁻¹, respectively; 30 minutes and 3 hours after a single 1g intravenous bolus injection of Flucloxacillin, the mean serum concentrations were 60 and 4 mg.l⁻¹ respectively. The administration of 2g Flucloxacillin by intravenous infusion over 20 minutes resulted in mean serum concentrations of 244 and 27.7 mg.l⁻¹ 15 minutes and 120 minutes respectively after the end of the infusion.

The percentage of a dose of intravenous Flucloxacillin recovered in urine in an 8 hour collection period varies from 60 to 76%.

About 95% of Flucloxacillin in the circulation is bound to plasma proteins. Flucloxacillin has been reported to have a plasma half-life of approximately one hour. The half-life is prolonged in neonates.

The serum half-life of Flucloxacillin in patients with severe kidney disease has been reported as 135 to 173 minutes. No significant difference in the half-life was found between patients on or off haemodialysis. Flucloxacillin is not removed by haemodialysis.

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. Up to 90% of an intramuscular dose is excreted in the urine within six hours. Only small amounts are excreted in the bile.

Flucloxacillin is unlikely to be excreted in breast milk to any significant extent. Similarly, placental transfer is unlikely to occur to any appreciable extent.

5.3 PRECLINICAL SAFETY DATA

N/A

6. PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENT(S)

None.

6.2 INCOMPATIBILITIES

None.

6.3 SHELF-LIFE

36 months

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 30°C in a dry place. Protect from light.

KEEP OUT OF REACH OF CHILDRE

6.5 NATURE AND CONTENTS OF CONTAINER

10 ml plain glass vials are packed in a carton along with an insert

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING

None

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER

FDA/SD.213-07996

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

7/22/2021

10. DATE OF REVISION / APPROVAL OF THE TEXT

08/2025