OXACIL

DESCRIPTION:
Oxacil Capsule 250mg : A size 2, scarlet/grey, marked 'CLOX/250' capsule.
Oxacil Granules 125mg/5ml : An almost white powder when reconstituted forms a yellow, fruity flavoured, homogenous suspension.

COMPOSITION:
Oxacil Capsule 250mg : Each capsule contains Cloxacillin 250 mg.
Oxacil Granules 125mg/5ml : Each 5 mL contains Cloxacillin 125 mg. Preservative: Sodium Benzoate 0.2%

PHARMACODYNAMICS:
Cloxacillin is an isoxazolyl penicillin and is resistant to staphylococcal penicillinase. It exerts its killing action on growing and dividing bacteria by inhibiting bacterial cell wall synthesis. Bacterial cell walls are held rigid and protected against osmotic rupture by peptidoglycan. Cloxacillin inhibits the final cross-linking stage of peptidoglycan production by binding to and inactivating transpeptidases, penicillin-binding proteins on the inner surface of the bacterial cell membrane. Other mechanisms involved include bacterial lysis by the inactivation of endogenous inhibitors of bacterial autolysins.

PHARMACOKINETICS:
Cloxacillin sodium is incompletely absorbed from the gastrointestinal tract following oral administration, and absorption is further reduced by the presence of food. Peak plasma concentrations of 7-1 4 mcg/mL have been observed 1-2 hours after a dose of 500 mg. Doubling the dose can double the plasma concentration.
Cloxacillin is widely distributed to most tissues and body fluids, including peritoneal fluid, blister fluid, urine, pleural fluid, middle ear fluid, intestinal mucosa, bone, gallbladder, lung, female reproductive tissues and bile.
Distribution into the cerebrospinal fluid is low in subjects with non- inflamed meninges. Therapeutic concentrations can be achieved in pleural and synovial fluids and in bone. Cloxacillin crosses the placenta and is excreted in breast milk. About 94% of cloxacillin is bound to plasma proteins. It has a half-life of 0.5-1 hour, and is prolonged in neonates. Thirty percent of the drug is metabolised in the liver and the unchanged drug and metabolites are excreted in the urine.

INDICATIONS:
Cloxacillin is used in the treatment of infections due to staphylococci-resistant to benzylpenicillin; it is also used for mixed streptococcal and staphylococcal infections when the staphylococcal are penicillin resistant. The following infections are indicated: Respiratory tract infection, Ear, Nose and Throat infection, Infected wounds, Septicaemia, Endocarditis, Staphylococcal enterocolitis. Osteomylitis. CLOXACILLIN is sometimes given with ampicillin for infection due to Beta-lactamase producing Gram-negative organisms since it may inhibit the destruction of ampicillin.

RECOMMENDED DOSAGE:
Adults: 250-500 mg every 6 hours before food. Usual adult prescribing limit: Up to 6 g daily.
Children: Infants and children up to 20 kg of body weight: 12.5 mg/kg body weight every 6 hours before food. Children over 20 kg body weight: 250-500 mg every 6 hours before food.

Instruction for reconstitution:
60ml: Add water to the mark on bottle (60ml). Shake well and make up to the mark if needed. Shake well before taking each dose.
100ml: Add water to the mark on bottle (100ml). Shake well and make up to the mark if needed. Shake well before taking each dose.

ROUTE OF ADMINISTRATION: For oral use.

CONTRAINDICATIONS:
Hypersensitivity to penicillins.

WARNINGS AND PRECAUTIONS:
Patients allergic to one penicillin may be allergic to other penicillins. Patients allergic to cephalosporins or cephamycins may be allergic to penicllins also. Desensitisation is necessary if treatment with penicillin is essential. Penicllins should be given with caution to patients with a history of allergy, especially to drugs or history of sensitivity to multiple allergens and patients with impaired renal function. Renal and hematological status should be monitored during prolonged and high-dose therapy. Care is also necessary when treating patients with syphilis due to risk of Jarisch-Herxheimer reactions. Contact with skin should be avoided since skin sensitisation may occur. Supra-infection with penicillin-resistant organisms including Pseudomonas or Candida may occur with prolonged use. Penicillins may cause pseudomembranous colitis in patients with history of gastrointestinal disease, especially antibiotic-associated colitis. Leukopenia or neutropenia is more likely to occur with prolonged therapy and severe hepatic function impairment. High urinary concentrations of a penicillin may produce false-positive or falsely elevated test results with copper sulphate tests (Benedict's, Clinitest or Fehling's). Glucose enzymatic tests (Clinistix or Testape) are not affected. False-positive result may occur during therapy with any penicillin in the direct antiglobulin (Coombs') tests.
Physiology/laboratory test values of alanine aminotransferase (ALT [SGPT]), alkaline phosphatase (ALP), aspartate aminotransferase (AST [SGOT]) and lactate dehydrogenase (LDH) may be increased.

Serious and occasionally fatal hypersensitivity reactions (including anaphylactoid and severe cutaneous adverse reactions) have been reported in patients receiving therapy with beta-lactams. Before initiating therapy with Cloxacillin, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins carbapenams or other beta-lactam agents. If an allergic reaction occurs, Cloxacillin must be discontinued immediately and appropriate alternative therapy instituted.

Toxicology
Carcinogenicity and mutagenicity
No documented long-term studies in animals that evaluate the carcinogenic and mutagenic potential of cloxacillin were available.

Pediatrics:
Penicillins have been used in pediatric and no pediatrics-specific problems have been documented to date. However, the incompletely developed renal function of neonates and young infants may delay the excretion of the drug.
Geriatrics:
Penicillins have been used in geriatric and no geriatric-specific problems have been documented to date. However, elderly patients may be more likely to have age- related renal function impairment, which may require and adjustment in dosage in patients receiving this drug.
Dental:
Prolonged use of cloxacillin may lead to the development of oral candidiasis.

INTERACTIONS WITH OTHER MEDICAMENTS:
Since bacteriostatic drugs may interfere with the bactericidal effect of cloxacillin in situations where a rapid bactericidal effect is necessary, it is best to avoid concurrent therapy with chloramphenicol, erythromycins, sulphonamides or tetracyclines.
There have been reports of reduced oral contraceptive effectiveness in women taking penicillins resulting in unplanned pregnancy. It is therefore prudent to advise patients to use an alternative or additional method of contraception. Cloxacillin may decrease clearance of methotrexate resulting in methotrexate toxicity.
Concurrent use of cloxacillin with hepatotoxic agents may increase the potential for hepatotoxicity. Probenecid decreases renal tubular secretion of cloxacillin and may increase risk of toxicity.

USE IN PREGNANCY AND LACTATION:

Pregnancy and Reproduction

(FDA Pregnancy Category B)

Cloxacillin crosses the placenta. Adequate and well-controlled studies in humans have not been done to determine whether penicillins are teratogenic; however, penicillins are widely used in pregnant women and problems have not been documented. Reproductive studies performed in the mouse, rat and rabbit given cloxacillin have revealed no evidence of impaired fertility or harm to the foetus.

Breast-feeding

Penicillins are distributed into breast milk. Although significant problems in human have not been documented, the use of penicillins by nursing mothers may lead to sensitisation, diarrhoea, candidiasis and skin rash in the infant.

SIDE EFFECTS/ ADVERSE EFFECTS:

Cloxacillin is generally well tolerated. Gastrointestinal effects like diarrhoea and nausea are common following oral administration of the drug. Headache, oral candidiasis (sore mouth and/or tongue, white patches in the mouth and/or on tongue) and vaginal candidiasis (vaginal itching and discharge) have been reported.

Allergic reactions, specifically anaphylaxis (fast and irregular breathing, puffiness and swelling around the face, shortness of breath, sudden, severe decrease in blood pressure), exfoliative dermatitis (red scaly skin), serum sickness-like reactions (skin rash, joint pain, fever), skin rash, hives or itching occasionally occurs.

Rare adverse effects reported include interstitial nephritis (fever, possible decreased urine output, skin rash), leukopenia and neutropenia (sore throat and fever). Hepatotoxicity has also been associated with cloxacillin.

Older patients and those receiving cloxacillin for more than 2 weeks are at greater risk. Pseudomembranous colitis and Clostridium difficile colitis (severe abdominal or stomach cramps and pain, abdominal tenderness, watery and severe diarrhoea which may be bloody, fever), which may occur during therapy or up to several weeks after discontinuation of the drug have also been reported. Seizures are more likely to occur in patients receiving high doses of the drug and/or patients with severe renal function impairment.

SYMPTOMS AND TREATMENT OF OVERDOSE:

There is no specific antidote for the treatment of cloxacillin overdose. Treatment should be symptomatic and supportive. Hemodialysis may aid in the removal of penicillins from the blood.

Serious anaphylactoid reactions require immediate emergency treatment with parenteral epinephrine, oxygen, intravenous corticosteroids and airway management (including intubation).

For Clostridium difficile colitis, mild cases may respond to discontinuation of the medicine alone. Moderate to severe cases may require fluid, electrolyte and protein replacement. In cases not responding to the above measures, oral doses of vancomycin, metronidazole or cholestyramine may be used.

Vancomycin: 125 mg 6 hourly for 5-10 days.
Metronidazole: 250-500 mg 8 hourly.
Cholestyramine: 4 g four times daily.

If diarrhoea occurs, administration of antiperistaltic antidiarrhoeals (opioids, diphenoxylate and atropine combination, loperamlde) is not recommended since they may delay the removal of toxins from the colon thereby prolonging and/or worsening the condition.

STORAGE CONDITIONS:

Oxacil Capsule 250mg:
Store in a dry place below 30°C. Protect from light.
Keep out of reach of children. *Jauhi daripada kanak-kanak.*

Oxacil Granules 125mg/ 5ml:
Keep container tightly closed.
Store in a dry place below 30°C. Protect from light.
Keep out of reach of children. *Jauhi daripada kanak-kanak.*
Store in the refrigerator after reconstitution. Discard 7 days after reconstitution. Consume within 12 months after opening the pouch.

PACKING / PACK SIZES:

Oxacil Capsule 250mg : Blister pack of 50x10's and 100x10's capsules in a box.
Oxacil Granules 125mg/ 5ml : 60ml and 100ml.

SHELF LIFE:

To refer to outer package.

PRODUCT REGISTRATION HOLDER & MANUFACTURER:

DUOPHARMA (M) SDN BHD
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41200 Klang, Selangor Darul Ehsan, MALAYSIA

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