Phylopen®

Flucloxacillin BP

COMPOSITION
Phylopen® 250 capsule : Each capsule contains Flucloxacillin Sodium BP equivalent to Flucloxacillin 250 mg.
Phylopen® DS capsule : Each capsule contains Flucloxacillin Sodium BP equivalent to Flucloxacillin 500 mg.
Phylopen® Dry syrup : Each 5 ml contains Flucloxacillin Sodium BP equivalent to Flucloxacillin 125 mg.
Phylopen® Forte Dry syrup : Each 5 ml contains Flucloxacillin Sodium BP equivalent to Flucloxacillin 250 mg.
Phylopen® 250 injection : Each vial contains sterile Flucloxacillin Sodium BP equivalent to Flucloxacillin 250 mg.
Phylopen® 500 injection : Each vial contains sterile Flucloxacillin Sodium BP equivalent to Flucloxacillin 500 mg.

PHARMACOLOGY
Flucloxacillin is a penicillin beta-lactam antibiotic used in the treatment of bacterial infections caused by susceptible, usually gram-positive, organisms. The name "penicillin" can either refer to several variants of penicillin available, or to the group of antibiotics derived from the penicillins. Flucloxacillin has *in vitro* activity against gram-positive and gram-negative aerobic and anaerobic bacteria.

Flucloxacillin is isoxazolyl penicillin which combined the properties of resistance to hydrolysis by penicillinase, gastric acid stability and activity against gram-positive bacteria. Flucloxacillin is a bactericidal antibiotic that is particularly useful against penicillinase-producing staphylococci.

Flucloxacillin kills bacterial cellwall, thus interfering with peptidoglycan synthesis. Peptidoglycan is a heteropolymeric structure that provides the cell wall with its mechanical stability. The final stage of peptidoglycan synthesis involves the completion of the cross-linking with the terminal glycine residue of the pentaglycin bridge linking to the fourth residue of the pentapeptide (D-alanine). The transpeptidase enzyme that performs this step is inhibited by Flucloxacillin. As a result the bacterial cell wall is weakened, the cell swells and then ruptures. Flucloxacillin is stable against hydrolysis by a variety of beta-lactamases, including penicillinases, and cephalosporinases and extended spectrum beta-lactamases Flucloxacillin resists the action of bacterial penicillinase probably because of the steric hindrance induced by the acyl side chain which prevents the opening of the β-lactam ring.

Pharmacokinetics
Flucloxacillin is well absorbed after either oral or intramuscular administration. Peak serum concentrations after oral administration of 250 mg -1 gm may range from 5-15 µg / mL after one hour. Similar concentrations at 30 minutes are achieved after intramuscular administration. Therapeutic concentrations persist for about 4 hours.
Although stable in acid, the presence of food in the stomach or small intestine will reduce absorption and so Flucloxacillin should be given on an empty stomach.
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 50% of an oral dose and 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.

INDICATION
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 skin conditions, e.g. ulcer, eczema and acne; infected wounds, infected burns, protection for skin grafts, otitis media and externa, impetigo.

Respiratory tract infections: pneumonia, lung abscess, empyema, sinusitis, pharyngitis, tonsillitis, and quinsy.
Other infections caused by Flucloxacillin-sensitive organisms: osteomyelitis, enteritis, endocarditis, urinary tract infections, meningitis, septicaemia.
Flucloxacillin is also indicated for use as a prophylactic agent during major surgical procedures where appropriate; for example, cardiothoracic and orthopaedic surgery.

DOSAGE AND ADMINISTRATION
Oral administration:
Oral doses should be administered half to one hour before meals.
Usual adult dosage (including elderly patients): 250-500 mg four times daily.
In severe infections, dosage should be doubled.
In osteomyelitis and endocarditis: up to 8 gm daily, in divided doses 6 to 8 hourly.
In case of secondary bacterial infection in chicken pox: Flucloxacillin 500 mg six hourly should be prescribed.

Usual children dosage:
2-10 years : half of the adult dose.
Under 2 years : quarter of the adult dose.

Parenteral administration:
Usual adult dosage (including elderly patients): Intramuscular Injection: 250-500 mg four times daily.
Intravenous Injection: 250 mg -1 gm four times daily by slow injection over 3 to 4 minutes or by intravenous infusion.
All systemic doses may be doubled in severe infections: doses up to 8 gm daily have been suggested for endocarditis or osteomyelitis.
Flucloxacillin has been used in other routes in conjunction with systemic therapy. It has been administered in a dose of 250 mg to 500 mg daily by intraarticular injection, dissolved if necessary in a 0.5% solution of lignocaine hydrochloride, and by intrapleural injection in a dose of 250 mg daily. Using powder for injection, 125 mg - 250 mg has been dissolved in 3 ml of sterile water and inhaled by nebuliser four times daily.

Usual children dosage:
2-10 years : half of the adult dose.
Under 2 years : quarter of the adult dose.
Dose adjustment in renal impairment :
As common with other penicillins, Flucloxacillin usage in patients with renal impairment does not usually require dosage reduction. However, in the presence of severe renal failure (creatinine clearance < 10 ml/min) a reduction in dose or an extension of dose interval should be considered.
Flucloxacillin is not significantly removed by dialysis and hence no supplementary dosages need to be administered either during or at the end of the dialysis period.

CONTRAINDICATION
Penicillin hypersensitivity.

SIDE EFFECT
Side effects as with other penicillin, are uncommon and mainly of a mild and transitory nature. Gastro-intestinal upsets (e.g. nausea, diarrhoea) and skin rashes have been reported. If skin rash occurs, treatment should be discontinued.

DRUG INTERACTION
The administration of probenecid with Flucloxacillin results in higher serum peak concentrations and prolongs the time that therapeutic concentrations of Flucloxacillin are achieved in serum. Physical incompatibility and/or loss of activity of Flucloxacillin in solution has been reported when given with gentamycin sulphate, streptomycin sulphate, vitamin Flucloxacillin should not be added to intravenous lipids, blood products and protein
hydrolysates or other proteinaceous fluids.

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.

WARNINGS AND PRECAUTIONS
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 Flucloxacillin therapy discontinued.
Serious anaphylactoid reactions require emergency treatment with adrenalin, oxygen and intravenous steroids. Airway management including tubation 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 AND LACTATION
The use of Flucloxacillin in pregnancy should be reserved for cases considered essential by the clinician. Use of the drug in the second and third trimesters may result in the sensitisation of the fetus. During lactation, trace quantities can be detected in breast milk.

STORAGE
Capsules: Store below 30°C. Protect from light and moisture.

Dry Syrups: Store below 30°C. Protect from light and moisture. After reconstitution, the syrup should be used within 7 days if kept at room temperature and within 10 days when stored in a refrigerator.

Injections: Store below 25°C. Protect from light and moisture.
Keep out of children's reach.

HOW SUPPLIED
Phylopen® 250 capsule : Box containing 5 x 10 / 10 x 10 / 100 x 10 capsules in strip pack.
Phylopen® DS capsule : Box containing 2 x 6 / 3 x 6 / 5 x 6 capsules in blister pack.
Phylopen ® Dry syrup : Bottle containing dry powder for reconstitution to 100 ml syrup.
Phylopen® Forte Dry syrup : Bottle containing dry powder for reconstitution to 100 ml syrup.
Phylopen® 250 injection : Box containing 5 / 10 / 20 blister packs, each containing one vial of **Phylopen** ® 250 injection and one 5 ml ampoule of Water for Injection.
Phylopen® 500 injection : Box containing 5 / 10 / 20 blister packs, each containing one vial of **Phylopen**® 500 injection and one 5 ml ampoule of Water for Injection.

SQUARE