For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory.

ZEFU POWDER FOR ORAL SUSPENSION 125MG/5ML

Cefuroxime Axetil for Oral Suspension

Description
White to off-white coloured free flowing flavoured powder, which upon reconstitution forms white to off-white coloured flavoured suspension.

Each 5ml (one teaspoonful) of reconstituted suspension contains Cefuroxime Axetil equivalent to Cefuroxime 125 mg.

Pharmacodynamics
Mode of action
Cefuroxime axetil owes its in vivo bactericidal activity to the parent compound cefuroxime. All cephalosporins (β-lactam antibiotics) inhibit cell wall production and are selective inhibitors of peptidoglycan synthesis. The initial step in drug action consists of binding of the drug to cell receptors, called Penicillin-Binding Proteins. After a β-lactam antibiotic has bound to these receptors, the transpeptidation reaction is inhibited and peptidoglycan synthesis is blocked. Bacterial lysis is the end result.

Mechanism of resistance
Bacterial resistance to cefuroxime may be due to one or more of the following mechanisms:

- hydrolysis by beta-lactamases. Cefuroxime may be efficiently hydrolysed by certain of the extended-spectrum beta-lactamases (ESBLs) and by the chromosomally-encoded (AmpC) enzyme that may be induced or stably derepressed in certain aerobic gramnegative bacterial species
- reduced affinity of penicillin-binding proteins for cefuroxime
- outer membrane impermeability, which restricts access of cefuroxime to penicillin binding proteins in gram-negative organisms
- drug efflux pumps

Methicillin-resistant staphylococci (MRS) are resistant to all currently available β-lactam antibiotics including cefuroxime.
Penicillin-resistant *Streptococcus pneumoniae* are cross-resistant to cephalosporins such as cefuroxime through alteration of penicillin binding proteins.
Beta-lactamase negative, ampicillin resistant (BLNAR) strains of H. influenzae should be considered resistant to cefuroxime despite apparent in vitro susceptibility. Strains of Enterobacteriaceae, in particular Klebsiella spp. and Escherichia coli that produce ESBLs (extended spectrum β-lactamase) may be clinically resistant to therapy with cephalosporins despite apparent in vitro susceptibility and should be considered as resistant.

Breakpoints:

According to the NCCLS (National Committee on Clinical Laboratory Standards) in 2001 the following breakpoints have been defined for cefuroxime axetil:

Enterobacteriaceae: ≤ 4 µg/ml susceptible, ≥ 32 µg/ml resistant

Staphylococcus spp.:≤ 4 µg/ml susceptible, ≥32 µg/ml resistant

Haemophilus spp.: ≤ 4 µg/ml susceptible; ≥ 16 µg/ml resistant

Streptococcus pneumoniae: ≤ 1 µg/ml susceptible, ≥ 4 µg/ml resistant

Streptococcus spp. other than S. pneumoniae:

Streptococcal isolates susceptible to penicillin (MIC90 0.12 µg/ml) may be considered susceptible to cefuroxime.

Susceptibility:
The prevalence of resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable.

Commonly susceptible species
Aerobes, Gram positive:
Staphylococcus aureus (methicillin-susceptible)
Coagulase-negative staphylococci (methicillin-susceptible)
Streptococcus agalactiae
Streptococcus pneumoniae
Streptococcus pyogenes
Aerobes, Gram negative :
Escherichia coli
Haemophilus influenzae

Klebsiella species
Moraxella catarrhalis
Proteus mirabilis
Proteus rettgeri
Anaerobes,
Peptococcus species
Peptostreptococcus species
Other organisms:
Borrelia burgdorferi .
Species for which resistance may be a problem
Acinetobacter species
Citrobacter species
Enterobacter species
Morganella morganii
Resistant
Bacteroides fragilis
Clostridium difficile
Enterococci
Listeria monocytogenes
Proteus vulgaris
Pseudomonas species
Serratia species

Pharmacokinetics
Absorption
The oral absorption of Cefuroxime axetil is good. Following oral administration, of Cefuroxime axetil, the drug is absorbed as the 1-(acetyloxy)ethyl ester from gastrointestinal tract and rapidly hydrolyzed to Cefuroxime by nonseptic esterases in the intestinal mucosa and blood.

Distribution
The apparent volume of distribution of Cefuroxime in healthy adults ranges from 9.3-15.8 L/1.73m2.

Elimination
In adult, serum or plasma half-life of Cefuroxime following oral administration of commercially available Cefuroxime axetil tables or oral suspension ranges from 1.2-1.6 hours. In neonates and children, the serum half-life of Cefuroxime is inversely proportional to age. Following oral administration of Cefuroxime axetil of oral suspension in children aged 13 months to 12 years of age, the serum half-life of Cefuroxime averages 1.4-16.1 hours. Cefuroxime is excreted mainly by the kidneys. In patients with renal impairment, the serum half-life of the drug is prolonged and generally ranges from 1.9-16.1 hours, depending on the degree of impairment.

Indications
Treatment of patients with infections caused by susceptible organisms, such as lower respiratory tract infections (pneumonia, acute and chronic bronchitis), upper respiratory tract infections (otitis media, sinusitis, tonsillitis and pharyngitis), urinary tract infections(eg. Pylonepheritis, cystitis and urethritis), skin and soft tissue infections and gonorrhea.

Recommended dose
Adults :
In bronchitis : 250 mg, twice daily.
Pneumonia : 500 mg, twice daily.
Urinary tract infection : 125 mg, twice daily.
Uncomplicated gonorrhoea : A single dose of 1 gm is recommended.

Children :
The usual dose is 125 mg (5ml) twice daily.

Children > 3 months : 125 mg (5ml) twice daily or 10 mg / kg bodyweight twice daily to a maximum of 250 mg (10ml) a day.

Children > 2 years (with otitis media) : 250 mg (10ml) twice daily or 15 mg/kg bodyweight twice daily to a maximum of 500 mg (20ml) a day.

The usual course of therapy is 7 days. Cefuroxime Axetil should be taken after food for optimum absorption.

Mode of Administration
Oral Administration:
Cefuroxime axetil oral suspension must be administered with food. Administration with food maximizes bioavailability of the drug. In paediatric patients, aged 3 months to 12 years who are unable to swallow tablets, cefuroxime maybe administered as the commercially available oral suspension.

Direction of Mixing
Tap the bottle to loosen the powder. slowly add boiled and cooled water upto the arrow mark on the label of bottle and shake well. Add water if necessary to adjust the volume upto the arrow mark.

Method of Reconstitution
Cefuroxime axetil powder for oral suspension should be reconstituted at the time of dispensing by adding the amount of water specified on the bottle to provide a suspension tapping the bottle to throughly loosen the powder for oral suspension, the water should be added in one portion and the suspension agitated well.

Contraindication
Patients with known allergy to cephalosporins.

Warning and Precautions
Prior to initiation of Cefuroxime therapy careful inquiry should be made concerning previous hypersensitivity reaction to cephalosporins and penicillins. Special care is indicated in patients who have experienced an anaphylactic reaction to penicillins. Cefuroxime therapy may result in overgrowth of nonsusceptible organisms (e.g *Candida enterococci, Clostridium difficile*) Cefuroxime should be used with caution in patients with history of GI disease, particularly colitis because *C.difficile* –associated diarrhea and colitis has been reported with use of Cefuroxime. Renal function should be monitored during therapy in seriously ill patients with renal impairment. Use of cefuroxime in children younger than 3 months of age has not been established.

Interactions with Other Medicaments
Simultaneous use of medicines enhancing the pH of the stomach decreases the bioavailability of cefuroxime axetil. It is recommended to avoid this combination.Since bacteriostatic drugs may interfere with the bactericidal action of cephalosporins, it is advisable to avoid giving tetracyclines, macrolides, or chloramphenicol in conjunction with cefuroxime axetil.

The concomitant administration of probenicid can produce higher and sustained concentrations of cefuroxime in the serum and in the bile. Cefuroxime may interfere with the determination of glucose in urine with copper containing reagentia (Benedict- or Fehling-solution, Clinitest). For the determination of blood- and plasma sugar levels in patients receiving cefuroxime axetil, the glucoseoxidase- or hexokinase method is recommended.

The use of cefuroxime axetil may be accompanied by a false positive Coombs test. This may interfere with the performance of cross matching tests with blood. Cephalosporin antibiotics at high dosage should be given with caution to patients receiving potent diuretics, aminoglycosides, or amphotericin as these combinations increases the risk of nephrotoxicity.

Pregnancy and Lactation
Pregnancy Category B: Cefuroxime has not revealed evidence of impaired fertility or harm to fetus. As with all drugs, because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed. Cefuroxime is excreted into the milk in small quantities. Hence caution should be taken when Cefuroxime is administered to nursing mothers.

Side Effects
Adverse reactions of Cefuroxime axetil have been generally mild and transient in nature. As with other cephalosporins, there have been rare reports of erythema multiforms, Stevens Johnson syndrome, toxic epidermal necrolysis and hypersensitivity reactions including skin rashes, urticaria, pruritus, drug fever, serum sickness and very rarely anaphylaxis. A small proportion of patients receiving Cefuroxime axetil have experienced gastrointestinal disturbance, including diarrhoea, nausea and vomiting. As with other spectrum antibiotics, there have been reports of pseudomembranous colitis. Headaches have also been reported Eosinophillia and transient increases of hepatic enzyme levels. [(ATL(SGPT), AST(SGOT) and LDH)] have been noted during Cefuroxime axetil therapy. There have been rare reports of thrombocytopenia and leucopenia which were rarely produced. As with other cephalosporins, jaundice has been reported very rarely.Cephalosporins as a class tend to be absorbed onto the surface of red-cell membranes and react with antibodies directed against the drug to produce a positive coomb's test (which can interfere with cross-matching of blood).

Symptoms and Treatment of Overdose
Overdose of cephalosporins may cause cerebral irritancy leading to convulsions. In case of overdose cefuroxime serum levels can be reduced by haemodialysis and peritoneal dialysis.

Storage
Store in a dry place, at a temperature not exceeding 25°C. Reconstituted suspension should be stored in refrigerator and should be used within 7 days.

Shelf life
18 months

Presentation:
30mL packed in Amber Glass Bottle with Measuring Cup.
50mL packed in Amber Glass Bottle with Measuring Cup.
60mL packed in Amber Glass Bottle with Measuring Cup.

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Product Registration Holder:
Unimed Sdn Bhd
53, Jalan Tembaga SD 5/2B,
Bandar Sri Damansara,
52200 Kuala Lumpur, Malaysia

Manufactured in India by:
FDC Limited
Village: Khol-Bhood, Tehsil: Nalagarh,
Baddi - 173 205, Dist - Solan, H.P.

2000007393

FDC Limited	LEAFLET	Minipharma Code no.	----------
Size	100(L) x 350 (H) mm		
Folded Size	25 x 87.5 MM		
No. of Folds	2 x 2		
GSM	60 gsm Maplitho		
Paper	60 gsm		
Specification No.	Maplitho		
Colour	■ TEXT IN BLACK		
Artwork Code: 2000007393		Supercedes A/W Code: 2000005654	
Location: MALAYSIA		Prepared On: 23-11-2018	
Reason for Change: Common PIL for 30 ml, 50 ml & 60 ml Pack Size.			