NATIONAL AGENCY FOR FOOD & DRUG ADMINISTRATION & CONTROL (NAFDAC)

Registration & Regulatory Affairs

(R & R)

Directorate

Product Name

FRESHCEF TABLET

(Cefuroxime Axetil Tablets USP 500 mg)

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

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SUMMARY OF PRODUCT CHARACTERISTICS (SMPC)

1. NAME OF THE MEDICINAL PRODUCT

FRESHCEF TABLET

(Cefuroxime Axetil Tablets USP 500 mg)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains :

Cefuroxime Axetil USP

Eq. to Cefuroxime 500 mg

3. PHARMACEUTICAL FORM

Film coated Tablet

4. CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Cefuroxime Axetil tablets are indicated for the treatment of pharyngitis/tonsillitis, Acute Bacterial Otitis Media, Acute Bacterial Maxillary Sinusitis, Acute Bacterial Exacerbations of Chronic Bronchitis, Uncomplicated Skin and Skin-structure Infections, Uncomplicated Urinary Tract Infections, Uncomplicated Gonorrhea, early Lyme disease (erythema migrans).

4.2 POSOLOGY AND METHOD OF ADMINISTRATION

Usual oral doses are 125 mg twice daily for uncomplicated urinary-tract infections and 250-500 mg twice daily for respiratory-tract infections. A suggested dose for children more than 3 months of age is 125 mg twice daily or 10 mg per kg body-weight twice daily to a maximum of 250 mg daily. Children over 2 years of age with otitis media may be given 250 mg twice daily or 15 mg per kg twice daily to a maximum of 500 mg daily.

Method of administration: Oral

4.3 CONTRAINDICATIONS

Known allergy to cephalosporin’s

Allergy to cephalosporins is an absolute contraindication.

4.4 WARNING AND PRECAUTION

Before therapy with Cefuroxime is instituted, careful inquiry should be made to determine whether the patient has had previous hypersensitivity reactions to cephalosporins, penicillins, or other drugs. This product should be given cautiously to penicillin sensitive patients. Antibiotics should be administered with caution to any patient who has demonstrated some form of allergy, particularly to drugs. If an allergic reaction to Cefuroxime occurs, discontinue the drug. Serious acute hypersensitivity reactions may require epinephrine and other emergency measures.

Although Cefuroxime rarely produces alterations in kidney function, evaluation of renal status during therapy is recommended, especially in seriously ill patients receiving the maximum doses. Cephalosporins should be given with caution to patients receiving concurrent treatment with potent diuretics as these regimens are suspected of adversely affecting renal function.

The total daily dose of Cefuroxime should be reduced in patients with transient or persistent renal insufficiency because high and prolonged serum antibiotic concentrations can occur in such individuals from usual doses.

As with other antibiotics, prolonged use of Cefuroxime may result in overgrowth of nonsusceptible organisms. Careful observation of the patient is essential. If super infection doses occur during therapy, appropriate measures should be taken.

4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

<u>Potentially hazardous interactions</u>

No interactions of this kind have been reported.

<u>Potentially useful interactions</u>

Cefuroxime dose produce in vitro synergies if combined with some other antibiotics such as aminoglycosides, but these are usually of limited clinical significance.

4.6 PREGNANCY AND LACTATION

Pregnancy

While all antibiotics should be avoided in the first trimester if possible, cefuroxime has been safely used in later pregnancy to treat urinary and other infections. The placental transfer of cefuroxime into the fetus was studied in 20 women and therapeutically active concentrations were found in the serum of infants for up to 6 h after delivery.

Lactation

Cefuroxime is excreted into the milk in small quantities. However, the possibility of sensitizing
the infant should be born in mind.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Patients experiencing visual disturbances, dizziness, vertigo, somnolence, or other central nervous system disturbances while taking Cefuroxime Axetil Tablets USP should refrain from driving or using machines.

4.8 UNDESIRABLE EFFECTS

Potentially life-threatening effects

As with all cephalosporin's, anaphylaxis is possible particularly in patients with a history of allergic reactions to cephalosporin's or penicillin, but is rare.

Cefuroxime Axetil is now recognized as causing significant risk of pseudomembranous colitis.

Severe or irreversible adverse effects

Cefuroxime treatment has been rarely associated with pseudomembranous colitis caused by overgrowth of Clostridium difficile in the bowel.

Symptomatic adverse effects

Cefuroxime Axetil has been associated with nausea and vomiting in a small number of patients.

The Jarisch–Herxheimer reaction, a transient immunological reaction lasting 1 to 2 days, has occurred in some patients with Lyme disease. Patients should be reassured that this is a common and usually self-limiting consequence of antibiotic treatment of Lyme disease.

Other effects

There have been reports of transient elevation of liver enzymes during therapy with cefuroxime, but these have usually returned to normal when therapy was stopped with no ill effect.

4.9 OVERDOSE AND SPECIAL ANTIDOTES

Excessively large doses of all cephalosporin's can cause cerebral irritation and may cause convulsions. This complication is unlikely to occur in routine practice unless the patient is in renal failure. Cefuroxime can be removed by hemodialysis or peritoneal dialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Cefuroxime is a semi-synthetic analog of cephalosporin C. It is active against a wide range of Gram-positive and Gram-negative bacteria, including staphylococcus aureus, streptococcus pyogenes, streptococcus pneumoniae, Neisseria spp., Haemophilus influenzae, and many common gram-negative hospital pathogens such as Escherichia coli, Klebsiella spp., and proteus mirabilis but not Pseudomonas aeruginosa or streptococcus faecalis. Among common hospital Gram-negative isolates, many strains of Enterobacter spp., Serratia spp., indole-positive proteus and acinetobacter spp. are resistant. In addition, many isolates of staph. epidermidis are resistant to cefuroxime. A glycopeptide such as vancomycin is the treatment of choice for serious staph. epidermidis infections. Cefuroxime has noteworthy activity against β-lactamase-producing strains of H. influenzae and N. gonorrhoeae, which are resistant to ampicillin and penicillin, respectively. Cefuroxime is more active in vitro against Gram-positive and Gram-negative organisms than earlier cephalosporins such as cephradine and cephaloridine. Newer cephalosporins such as cefotaxime and ceftazidime are more active than cefuroxime against many Gram-negative isolates, but have reduced active against Gram-positive organisms such as staph. Aureus. Overall, cefuroxime sodium is comparable in activity to cefamandole. In comparison with cefoxitin it has increased activity against Gram-positive organisms and Enterobacter spp., is less active against anaerobic organisms.

Cefuroxime axetil undergoes complete hydrolysis during absorption to free cefuroxime. Its in vitro microbiological activity is the same as the parent cefuroxime. Cefuroxime axetil is best compared with cefaclor and augmentin. Cefuroxime axetil is more active against β-lactamase-producing H. influenzae than cefaclor (as is augmentin), but has no worthwhile activity against anaerobes, e.g. Bacteroides fragilis, in comparison with augmentin. It has a broader spectrum of activity than early cephalosporins such as cephalexin. There are, however, newer oral agents, e.g. cefpodoxime and cefixime, which are more active in vitro than cefuroxime and cefixime axetil.

Cefuroxime is a bactericidal antibiotic that inhibits bacterial cell wall synthesis like other β-lactam antibiotics. As with other β-lactam antibiotics, cefuroxime interferes with the transpeptidation process binding the bacterial cell wall, weakening the cell wall to produce non-viable filaments. Cefuroxime also binds to penicillin-binding protein 3, which is involved in the formation of the peptidoglycan bacterial cell wall, leading to lysis of the organism. Its broad spectrum of activity is in part owing to its stability to some of the commoner bacterial β-lactamases.

5.2 PHARMACOKINETIC PROPERTIES

The preferred analytical method is by bioassay, using agar diffusion and a Gram-negative organism as indicator, with the usual lower limit of sensitivity around 0.06 mg. Cefuroxime has a plasma half-life of approximately 75 min in subjects with normal renal function.

It is about 33% bound to serum. The volume of distribution after a 1 g dose is 11.1 - 13.71 per 1.73 m^2. There were wide variations in absorption of Cefuroxime axetil in early studies and some early papers refer to formulations not now used. The final formulation developed gives peak serum concentrations of 7-10 mg if taken before food. Cefuroxime axetil is completely hydrolyzed in the intestine to Cefuroxime; its pharmacokinetics are then the same as Cefuroxime sodium, but the serum level is much closer to the MIC of important pathogens than the parent form. The drug is primarily eliminated by the kidneys, with urinary recovery about 35% and an elimination half-life of 1.5 h. The drug crosses the placenta and can also be detected in breast milk.

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Oral absorption	
cefuroxime	Not relevant
Cefuroxime axetil	Good
Presystemic metabolism	
cefuroxime	Not relevant
Cefuroxime axetil	Hydrolyzed to cefuroxime
Plasma half life	
Cefuroxime	75 min
Volume of distribution	11.1 – 12.2
(both drugs)	13.71.1.73 m^{-2}
Plasma protein binding	
(both drugs)	30%

Concentrations - effect relationship

The therapeutic effect of Cefuroxime sodium, as with all antibiotics, depends on achieving a level of antibiotic in excess of the MIC of the causative organism. This is relatively easily achieved with an infection in urine or blood, but is more difficult at enclosed sites such as abscesses or gallbladder infection. Fewer data are available for Cefuroxime axetil. Serum levels are in excess of the MIC of many pathogens, but information on its penetration into sputum and other sites is still needed.

Metabolism

Cefuroxime is rapidly excreted in high concentration through the kidney with over 90% of the given dose recovered in the urine within 6 h of injection. Renal clearance is equally divided between clearance through tubules and glomerular filtration: mean drug: creatinine clearance ratios were 1:1 to 1:3, suggesting half the drug is filtered and half is actively secreted by the kidney tubules. Virtually all Cefuroxime is excreted in the urine, with no detectable enter hepatic circulation. High pressure liquid chromatography studies of Cefuroxime in urine samples showed that over 95% is excreted as unchanged Cefuroxime. There are no known pharmalogically active metabolites.

Cefuroxime Axetil is better absorbed if taken after food, when 50% can be removed in the urine. No unhydrolysed ester is detected in serum.

5.3 PRECLINICAL SAFETY DATA

Cefuroxime, like many other β-lactam antibiotics, shows little evidence of human or animal toxicity. There are no reports of toxicological results in animals that are of human significance. There was no evidence of nephrotoxicity in mice given up to 6 g.kg Cefuroxime subcutaneously. There was no evidence of teratological effects in mice or rabbits. Long-term carcinogenicity tests have not been carried out. Cefuroxime axetil has a similar toxicology profile to the parent drug.

6. PHARMACEUTICAL PARTICULARS

None

6.1 INCOMPATIBILITIES

Not applicable.

6.2 SHELF LIFE

3 years

6.3 SPECIAL PRECAUTIONS FOR STORAGE

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

6.4 NATURE AND CONTENTS OF CONTAINER

Alu-Alu pack of 1 x 10 tablets in a carton.

6.5 SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER SPECIAL HANDLING

None

7. Manufactured by:

ALPA LABORATORIES LTD.
33/2, A. B. Road, Pigdamber-
453 446, Indore (M.P.)

FRESHCEF TABLET
(Cefuroxime Axetil Tablets USP 500 mg)

8. Marketing Authority:

FRESHBORN INDUSTRIES LTD.

Plot 18, Jesus Estate, Ijegun

Satellite Town, Lagos State, Nigeria.