FIRST FOLD SHOULD BE HORIZONTAL & REMAINING VERTICAL

ZOCEF TABLETS 250 mg/500 mg

Cefuroxime Axetil Tablets BP

COMPOSITION
Each film-coated tablet contains:
Cefuroxime Axetil EP equivalent to Cefuroxime 250 mg/500 mg
Colour : Titanium Dioxide BP

PRODUCT DESCRIPTION
White to off-white, capsule shaped, film coated tablets with break line on one side and plain on other side.

DESCRIPTION
Zocef Tablets contain Cefuroxime as Cefuroxime Axetil. Cefuroxime Axetil is a semi-synthetic, broad-spectrum cephalosporin antibiotic for oral administration. Cefuroxime Axetil is in the amorphous form.
Zocef Tablets are film-coated and contain the equivalent of 500 mg of Cefuroxime as Cefuroxime Axetil. **Zocef** Tablets contain the inactive ingredients colloidal silicon dioxide, croscarmellose sodium, Hydroxy propyl methyl cellulose, microcrystalline cellulose, propylene glycol, sodium lauryl sulfate, Calcium Stearate, calcium Carbonate, Cross povidone, and titanium dioxide.
Chemically, Cefuroxime Axetil, the 1-(acetyloxy) ethyl ester of cefuroxime, is (*RS)* -1-hydroxyethyl (6 *R*, 7 *R*)-7-[2-(2-furyl) glyoxylamido]-3-(hydroxymethyl)-8-oxo-5-thia-1-azabicyclo [4.2.0]oct-2-ene-2-carboxylate, 7 2 -(*Z*)-(*O* -methyl-oxime), 1-acetate 3-carbamate. Its molecular formula is $C_{20}H_{22}N_4O_{10}S$ and it has a molecular weight of 510.48.

PHARMACOLOGY AND PHARMACOKINETICS
Approximately 50% of serum Cefuroxime is bound to protein. Serum pharmacokinetic parameters for **Zocef** Tablets are shown in Table 1.

Table 1. Postprandial Pharmacokinetics of Cefuroxime Administered as Tablets to Adults *

Dose † (Cefuroxime Equivalent)	Peak Plasma Concentration (mcg/mL)	Time of Peak Plasma Concentration (hr)	Mean Elimination Half-Life (hr)	AUC (mcg-hr mL)
125 mg	2.1	2.2	1.2	6.7
250 mg	4.1	2.5	1.2	12.9
500 mg	7.0	3.0	1.2	27.4

* Mean values of 12 healthy adult volunteers.

† Drug administered immediately after a meal.

Food Effect on Pharmacokinetics: Absorption of the tablet is greater when taken after food (absolute bioavailability of **Zocef** Tablets increases from 37% to 52%). Despite this difference in absorption, the clinical and bacteriologic responses of patients were independent of food intake at the time of tablet administration in 2 studies where this was assessed.
Renal Excretion: Cefuroxime is excreted unchanged in the urine; in adults, approximately 50% of the administered dose is recovered in the urine within 12 hours. Because Cefuroxime is renally excreted, the serum half-life is prolonged in patients with reduced renal function.

INDICATIONS
Upper respiratory tract infections eg, ear, nose and throat infections ie, otitis media, sinusitis, tonsillitis and pharyngitis. Lower respiratory tract infections eg, pneumonia, acute bronchitis and acute exacerbations of chronic bronchitis. Genitourinary tract infections eg, pyelonephritis, cystitis and urethritis. Skin and soft-tissue infections eg, furunculosis, pyoderma and impetigo. Gonorrhoea, acute uncomplicated gonococcal urethritis and cervicitis. Where appropriate Zocef is effective when used following initial parenteral cefuroxime sodium in the treatment of pneumonia and acute exacerbations of chronic bronchitis.

DOSAGE AND ADMINISTRATION
The usual course of therapy is 7 days (Range 5-10 days).
Zocef should be taken after food for optimum absorption.
Adults:
Most Infections: 250 mg twice daily.
Urinary Tract Infections: 125 mg twice daily.
Mild to Moderate Lower Tract Infections eg, Bronchitis: 250 mg twice daily.
More Severe Lower Tract Infections (or if pneumonia is suspected): 500 mg twice daily.
Pyelonephritis: 250 mg twice daily.
Uncomplicated Gonorrhoea: Single dose of 1 g.
Sequential Therapy:
Pneumonia: 1.5 g. Cefuroxime sodium 2-3 times a day (IV or IM) for 48-72 hrs followed by 500 mg twice a day Zocef (cefuroxime axetil) oral therapy for 7-10 days.
Acute Exacerbations of Chronic Bronchitis: 750-mg Cefuroxime sodium 2-3 times a day (IV or IM) for 48-72 hrs, followed by 500 mg twice a day Zocef (cefuroxime axetil) oral therapy for 5-10 days.
Duration of oral therapy is determined by the severity of the infection and the clinical status of the patient.
Children: **Most infections:** 125 mg (1 x 125 mg tab) twice daily, to a maximum of 250 mg daily.
Children ≥ 2 years with otitis media or where appropriate, with more severe infections: 250 mg (1 x 250-mg tab or 2 x 125-mg tab) twice daily, to a maximum of 500 mg daily.
Zocef tablets should not be crushed and are therefore unsuitable for treatment of patients eg, younger children, who cannot swallow tablets.
There is no experience of using Zocef in children <3 years.

WARNINGS AND PRECAUTIONS
Before therapy with **Zocef** tablets is instituted, careful inquiry should be made to determine whether the patient has had previous hypersensitivity reactions to Cefuroxime, other cephalosporins, penicillins or other drugs. If this product is to be given to penicillin-sensitive patients, caution should be exercised because cross-hypersensitivity among beta-lactam antibiotics has been clearly documented and may occur in up to 10% of patients with a history of penicillin allergy. If a clinically significant allergic reaction to Cefuroxime occurs, discontinue the drug and institute appropriate therapy. Serious acute hypersensitivity reactions may require treatment with epinephrine and other emergency measures, including oxygen, intravenous fluids, intravenous antihistamines, corticosteroids, pressor amines, and airway management, as clinically indicated.
Pseudomembranous colitis has been reported with nearly all antibacterial agents, including Cefuroxime, and may range from mild to life threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhea subsequent to the administration of antibacterial agents.
Treatment with antibacterial agents alters normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by *Clostridium difficile* is one primary cause of antibiotic-associated colitis.
After the diagnosis of pseudomembranous colitis has been established, appropriate therapeutic measures should be initiated. Mild cases of pseudomembranous colitis usually respond to drug discontinuation alone. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation, and treatment with an antibacterial drug effective against *Clostridium difficile.*

PRECAUTIONS
General: As with other broad-spectrum antibiotics, prolonged administration of Cefuroxime Axetil may result in overgrowth of nonsusceptible micro-organisms. If superinfection occurs during therapy, appropriate measures should be taken.
Cephalosporins, including Cefuroxime Axetil, should be given with caution to patients receiving concurrent treatment with potent diuretics because these diuretics are suspected of adversely affecting renal function.

Cefuroxime Axetil, as with other broad-spectrum antibiotics, should be prescribed with caution in individuals with a history of colitis. The safety and effectiveness of Cefuroxime Axetil have not been established in patients with gastrointestinal malabsorption. Patients with gastrointestinal malabsorption were excluded from participating in clinical trials of Cefuroxime Axetil.
Cephalosporins may be associated with a fall in prothrombin activity. Those at risk include patients with renal or hepatic impairment or poor nutritional state, as well as patients receiving a protracted course of antimicrobial therapy, and patients previously stabilized on anticoagulant therapy. Prothrombin time should be monitored in patients at risk and exogenous Vitamin K administered as indicated.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Although lifetime studies in animals have not been performed to evaluate carcinogenic potential, no mutagenic activity was found for Cefuroxime Axetil in a battery of bacterial mutation tests. Positive results were obtained in an in vitro chromosome aberration assay; however, negative results were found in an in vivo micronucleus test at doses up to 1.5 g/kg. Reproduction studies in rats at doses up to 1,000 mg/kg/day (9 times the recommended maximum human dose based on mg/m^2) have revealed no impairment of fertility.
Pediatric Use: The safety and effectiveness of Cefuroxime Axetil have been established for pediatric patients aged 3 months to 12 years for acute bacterial maxillary sinusitis based upon its approval in adults. Use of Cefuroxime Axetil in pediatric patients is supported by pharmacokinetic and safety data in adults and pediatric patients, and by clinical and microbiological data from adequate and well-controlled studies of the treatment of acute bacterial maxillary sinusitis in adults and of acute otitis media with effusion in pediatric patients. It is also supported by post-marketing adverse events surveillance.
Geriatric Use: Of the total number of subjects who received Cefuroxime Axetil in 20 clinical studies of Cefuroxime Axetil, 375 were 65 and over while 151 were 75 and over. No overall differences in safety or effectiveness were observed between these subjects and younger adult subjects. The geriatric patients reported somewhat fewer gastrointestinal events and less frequent vaginal candidiasis compared with patients aged 12 to 64 years old.

CONTRAINDICATIONS
Cefuroxime Axetil Tablets are contraindicated in patients with known allergy to the cephalosporin group of antibiotics.

DRUG INTERACTIONS
Drug/Laboratory Test Interactions: A false-positive reaction for glucose in the urine may occur with copper reduction tests (Benedict's or Fehling's solution or with CLINI-TEST ® tablets), but not with enzyme-based tests for glycosuria (e.g., CLINISTIX ®). As a false-negative result may occur in the ferricyanide test, it is recommended that either the glucose oxidase or hexokinase method be used to determine blood/plasma glucose levels in patients receiving Cefuroxime Axetil. The presence of Cefuroxime does not interfere with the assay of serum and urine creatinine by the alkaline picrate method.

Drug/Drug Interactions: Concomitant administration of probenecid with **Zocef** tablets increases the area under the serum concentration versus time curve by 50%. The peak serum Cefuroxime concentration after a 1.5 g. single dose is greater when taken with 1 g. of probenecid (mean = 14.8 mcg/mL) than without probenecid (mean = 12.2 mcg/mL).
Drugs that reduce gastric acidity may result in a lower bioavailability of Cefuroxime Axetil compared with that of fasting state and tend to cancel the effect of postprandial absorption.

PREGNANCY AND LACTATION
Pregnancy: ***Teratogenic Effects:*** Pregnancy Category B. Reproduction studies have been performed in mice at doses up to 3,200 mg/kg/day (14 times the recommended maximum human dose based on mg/m^2) and in rats at doses up to 1,000 mg/kg/day (9 times the recommended maximum human dose based on mg/m^2) and have revealed no evidence of impaired fertility or harm to the fetus due to Cefuroxime Axetil. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.
Labor and Delivery: Cefuroxime Axetil has not been studied for use during labor and delivery.
Nursing Mothers: Because Cefuroxime is excreted in human milk, consideration should be given to discontinuing nursing temporarily during treatment with Cefuroxime Axetil.

SIDE EFFECTS

Table 3. Adverse Reactions - Zocef Tablets Multiple-Dose Dosing Regimens - Clinical Trials

Incidence >/=1%	Diarrhea/loose stools	3.7%
	Nausea/vomiting	3·0%
	Transient elevation in AST	2.0%
	Transient elevation in ALT	1.6%
	Eosinophilia	1.1%
	Transient elevation in LDH	1.0%
Incidence <1% but >0.1%	Abdominal pain	
	Abdominal cramps	
	Flatulence	
	Indigestion	
	Headache	
	Vaginitis	
	Vulvar itch	
	Rash	
	Hives	
	Itch	
	Dysuria	
	Chills	
	Chest pain	
	Shortness of breath	
	Mouth ulcers	
	Swollen tongue	
	Sleepiness	
	Thirst	
	Anorexia	
	Positive Coombs test	

SYMPTOMS AND TREATMENT OF OVERDOSE
Overdosage of cephalosporins can cause cerebral irritation leading to convulsions. Serum levels of cefuroxime can be reduced by hemodialysis and peritoneal dialysis.

STORAGE CONDITION
Store in a well closed container protected from light, not exceeding 30°C.

SUPPLY
Zocef 250 : Box of 10/50/100 Tablets
Zocef 500 : Box of 6/10/50/100 Tablets

Manufactured by :
ALKEM LABORATORIES LTD.
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