For the use of a Registered Medical Practitioner or a Hospital or a Laboratory Only

Cefuroxime Axetil Tablets IP

Cefuzrom™ 500
Tablets

COMPOSITION :
Each film coated tablet contains :
Cefuroxime Axetil IP
eq. to Anhydrous Cefuroxime 500 mg **Colour :** Titanium Dioxide IP

PHARMACEUTICAL FORM Film Coated tablet

THERAPEUTIC INDICATIONS
Indicated for the treatment of lower and upper respiratory tract infections,UTI, gynecological inffectionsskin and d soft tisinf infections.

POSOLOGY AND METHOD OF ADMINISTRATION Posology
The usual course of therapy is seven days (may range from five to ten days). The recommended dosage are as follows:
Table 1. Adults and children (≥40 kg)

Indication	Dosage
Acute tonsillitis and pharyngitis, ace bactcterial sinusitis	250 mg twice daily
Acute otitis media	500 mg twice daily
Acute exacerbations of chonic brronchitis	500 mg twice daily
Cystitis	250 mg twice daily
Pyelonephritis	250 mg twice daily
Uncomplicated skin and soft tissue infections	250 mg twice daily
Lyme disease	500 mg twice daily for 14 days (range of 10 to 21 days)

Table 2. Children (<40 kg)

Indication	Dosage
Acute tonsillitis and pharyngitis, acute bacterial sinusitis	10 mg/kg twice daily to a maximum of 125 mg twice daily
Children aged two years or older with otitis media , where appropriate, with more severe infnfections	15 mg/kg twice daily to a maximum of 250 mg twice daily
Cystitis	15 mg/kg twice daily to a maximum of 250 mg twice daily
Pyelonephritis	15 mg/kg twice daily to a maximum of 250 mg twice daily for 10 to 14 days
Uncomplicated skin and soft tissue infections	15 mg/kg twice daily to a maximum of 250 mg twice daily
Lyme disease	15 mg/kg twice daily to a maximum of 250 mg twice daily for 14 days (10 to 21 days)

There is no experience of using Cefuroxime axetilin children under the age of 3 months.
Renal impairment
The safety and efficacy of cefuroxime axaxetin in patiewith renal failure have not been established.
Cefuroxime is primarily excreted by the kidneys. In patientswith markedly impaired renal functioit is recommended that the dosage of cefuroxime should be reduced to compensate for its slower excretion.Cefuroxime is effffecely removed by dialysis.

Table 3. Recommended doses for Cefuroxime axetil *in renal impairment:*

Creatinine cleaance	$T_{1/2}$ (hrs)	Recommended dosage
≥30 mL/min/1.73 m^2	1.4-2.4	no dose adjustment necessary (standard dose of 125 mg to 500 mg given twice daily)
10-29 mL/min/1.73 m^2	4.6	standard individual dose given every 24 hours
<10 mL/min/1.73 m^2	16.8	standard individual dose given every 48 hours
Patients on haemodialysis	2–4	a further standard individual dose should be given at the end of each dialysis

Hepaticimpairment
There are no data available for patientswith hepatiimpairment. Since cefuroxime is primarily eliminated by the kidney, the presence of f hepatic dysfunctis expected to have no effect on the pharmacokineticsof cefuroxime.
Method of administration: Oral use only
Cefuroxime tablets should be taken afer food for optimum absorption.
Cefuroxime tablets should not be crushed and are therefore unsuitable for treatment of patientswho cannot swallow tablets. In children Cefuroxime axxetioral suspension may be used.

CONTRAINDICATIONS
It is contraindicated in patientswith known hyperrsensitivitto the e ace substance or to any of the excipients.
History of severe hypersensitivity(e.g. anaphhylactir reactioto any other type of beta-lactam am antierial agent (Penicillins, Monobactams and Carbapenems).

SPECIAL WARNINGS AND PRECAUTIONS FOR USE Hypersensitivityrreactions
Special care is indicated in patients who hve experienced an allergic rreaction to penicillins or other ba-lactctam antibiotics because e is a risk of crf cross-sensit. As with all betalactam antibacerial agents, serious and occasionally fatal hyperrsensitivitr reactiohave been reported. In case of severe hyperpersensitivrty reactitreatment with cefuroxime must be discontinuedimmediately and adequate emergency measures must be initied.
Before beginning treatment, it should be established whether the patienthas a history of severe hyperrsensitivitr reactioto cefuroxime, to other cephalosporins or to any other type of beta-lactam agent. Cautionshould be used if cefuroxime is given to patientwith a history of non-severe hyperersensitivito other beta-lactam agents.
Jarisch-Herxheimer reaction
The Jarisch-Herxheimer reactionhas been seen following cefuroxime axxetitreatment of Lyme disease. It results directly from the bactericidal l activiof cefuroxime ax axeon the the caue bacteria of Lyme disease, the spirochaete *Borrelia burgdorferi.* Patientsshould be reassured that this is a common and usually selff-limitinconsequence of f antibiotreatment of Lyme disease.
Overgrowth of non-susceptiblemicroorganisms
As with other antibioticsuse of cefuroxime axaxetmay result in the overgrowth of Candida. Prolonged use may also result in the overgrowth of other er non-susceptimicroorganisms (e.g.
enterococci and *Clostridium difficile*), which may require interruptionof treatment.
Antibacerial agent–associated pseudomembranous colitihave been reported with nearly all l antiberial agents, including cefuroxime and may range in severity from mild to life threatening. This diagnosis should be considered in patientswith diarrhoea during or subsequent to the administrratioof cefuroxime. . Discontinuatof therapy with cefuroxime and the administrationof specific treatment for *Clostridium difficile* should be considered. Medicinal products that inhibit peristalsis should not be given.
Interference with diagnostictests
The development of a positie Coombs' Test associated with the use of cefuroxime may interfere with cross matching of blood.
As a false negatie result may occur in the ferricyanide test, it is recommended that either the glucose oxidase or hexokinase methods are used to determine blood/plasma glucose levels in patientsreceiving cefuroxime axxetil.

DRUG INTERACTIONS
Drugs which reduce gastric acidity may result in a lower bioavailability of cefuroxime axetilcompared with that of the fasstinstate and tend to cancel the effect of enhanced ed absorption afer food. Cefuroxime is excreted by glomerular filtrtratiand tubular secrecretiConcomitant use of probenecid is not recommended. Concurrent administristraof probenecid significantly increases the peak concentrrationarea under the serum concentrtration tcurve and and eliminahalf-life of cefuroxime. Concomitant use with oral oral anticoagumay give rise to increased INR.

FERTILITY, PREGNANCY AND LACTATION Pregnancy
There are limited data from the use of cefuroxime in pregnant women. Studies in animals have shown no harmful effects on pregnancy, embryonal or foetal development, parturitioor postnatal development. Cefuroxime axetilshould be prescribed to pregnant women only if the benefit outweighs the risk.
Breasteeding
Cefuroxime is excreted in human milk in small quantitiesAdverse effects at therherapeudoses are not expected, although a risk of diarrhoea and fungus inf infecof the mucous membranes cannot be excluded. Breasteeding might have to be discontinuedue to these effects. The possibility of of sensitisashould be taken into account. Cefuroxime should only be used during breasteeding aer benefit/risk assessment by the physician in charge.
Fertility
There are no data on the effects of cefuroxime axxetion f fertiliin humans. Repreprodue studies in animals have shown no effects on f on fer.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES
No studies on the effects on the ability to drive and use machines have been performed. However, as this medicine may cause dizziness, patientshould be warned to be e cautiowhen driving or operatingmachinery.

UNDESIRABLE EFFECTS
Fixed drug eruption(FDE) has been reported with cephalosporin class ffformulations.
The most common adverse reactionsare *Candida* overgrowth, eosinophilia, headache, dizziness, gastrointesstinadisturbances and transient rise in liver enzymes.
The frequency categories assigned to the adverse reactionsbelow are esstimes, as for most r reactiosuitable data (for example from placebo-controlled studies) for or calculatincidence were not available. In addition,the incidence of adverse rreactionassociated with cefuroxime axaxetmay vary according to the he indication.
Data from large clinical studies were used to determine the frequency of very common to rare undesirable effects. The frequencies assigned to all other undesirable effects (i.e. those occurring at <1/10,000) were mainly determined using post-marketingdata and refer to a rreportinrate rather than true frequency. Placebo-controlled trial data were not available.
Where incidences have been calculated from clinical trial data, these were based on drug-related (investiator assessed) data. Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.
Treatment related adverse reactions,all grades, are listed below by MedDRA body system organ class, frequency and grade of severity. The following convventiohas been n utilisfor the classificatioof frequency: very common ≥ 1/10; common ≥ 1/100 to < 1/10, uncommon ≥ 1/1,000 to < 1/100; rare ≥ 1/10,000 to < 1/1,000; very rare < 1/10,000 and not known (cannot be estimaed from the available data).

System organ class	Common	Uncommon	Not known
Infections and infestations	Candida overgrowth		*Clostridium difficile*overgrowth
Blood and lymphatic ystem disorders	eosinophilia	positive Coombs' test, thombocytopenia, leukopenia (sometimes pofound)	haemolytic anaemia
Immune system disorders			drug fever, serum sickness, anaphylaxis, Jarisch-Herxheimer reaction
Nervous system disorders	headache, dizziness		
Gastrointestinal disoders	diarrhoea, nausea, abdominal pain	vomiting	pseudomembranous colitis
Hepatobiliary disorders	transient increases of hepatic enzyme levels		jaundice (predominantly cholestatic), hepatitis
Skin and subcutaneous tissue disoders		skin rashes	urticaria, pruritus, erythema multorme, Stevens-Johnson syndrome, toxic epidermal necrolysis (exanthematic necolysis) (see Immune system disorders), angioneurotic oedema
Description of selected adverse reactions Cephalosporins as a class tend to be absorbed onto the surface of red cells membranes and react with antibodies diected against the drug to produce a positive Coombs' test (which can interere with cross-matching of blood) and very rarely haemolytic anaemia. Transient rises in serum liver enzymes have been observed which are usually reversible.			

Paediatric population
The safety profile for cefuroxime axxetiin children is consistent with the profile in adults.
***Reportingof side effects or suspected adverse reaction*:** If you experience any side effects, talk to your doctor or pharmacist or report to indiadrugsafety@akums.in. You can also report side effects directly via the NationaPharmacovigilance Programme of India by calling on 1800 180 3024. By r reportiside effects, you can help provide more inf informaon the safety of this product.

OVERDOSE
Overdose can lead to neurological sequelae including encephalopathy, convulsions and coma. Symptoms of overdose can occur if the dose is not reduced appropriately in patientswith renal impairment.
Serum levels of cefuroxime can be reduced by haemodialysis and peritoneal dialysis.

PHARMACOLOGICAL PROPERTIES
Pharmacodynamic properties
Pharmacotherapeuticgroup: antibaerials for systemic use, , second-generaticephalosporins.
Mechanism of action
Cefuroxime axetilundergoes hydrolysis by esterase enzymes to the acte e antibiotcefuroxime.
Cefuroxime inhibits bacterial cell wall synthesis following atachment to penicillin binding proteins (PBPs). This results in the intterruptioof cell wall l (peptidocan) biosynthesis, which leads to bacterial cell lysis and death.
Cefuroxime axetilbreakpoints
Minimum inhibitory concentration(MIC) breakpoints established by the European Commiee on n Antimobial al SusceptibilTes Tes(EUCAST) are as follows:

Microorganism	Breakpoints (mg/L)	
	S	R
Enterobacteriaceae [1,2]	≤8	>8
Staphylococcus spp.	Note[3]	Note[3]
*Streptococcus*A, B, C and G	Note[4]	Note[4]
Streptococcus pneumoniae	≤0.25	>0.5
Moraxella catarrhalis	≤0.125	>4
Haemophilus influenzae	≤0.125	>1
Non-species related breakpoints[5]	IE[5]	IE[5]

1 The cephalosporin breakpoints for *Enterobacteriaceae*will detect all clinically important resistance mechanisms (including ESBL and plasmid mediated AmpC). Some ains that produce beta-lactamases are susceptible or intermediate to 3rd or 4th generation cephalosporins with these beakpoints and should be reported as found, i.e. the presence or absence of an ESBL does not in itself influence the categorizzation of susceptibilit. In many areas, ESBL detection and chaacterizzation isecommended or mandatory for infnfection cool purposes.
2 Uncomplicated UTI (cystitis) on.
3 Susceptibility of stapylococci to cephalosporins is inferred frrom the methicillin susceptibilityxcept f for cazidme and cefixime and ceftibuten, which do not ve breakpoints and should not be used for staphylococcal infections.
4 The beta-lactam susceptibility of beta-haemolytic steptococci groups A, B, C and G is inferred frrom the penicillin susceptibili.
5 insufficient evidence that the species in question is a good get for therapy with the drug.
An MIC witha comment but without an accompanying S or R-categorization my be reported.

S=susceptible,R=resistant
Microbiological susceptibility
The prevalence of acquired resistance may vary geographically and with timefor selected species and local inffomatioon resistance is desirable, , particularwhen tr treatsevere infections.As necessary, expert advice should be sought when the local prevalence of resistance is such that the utilitof cefuroxime axaxetin at least some types of infinfectiis questionable.
Cefuroxime is usually actie against the following microorganisms *in vitro*.

Commonly susceptible species
Gram-positive aeobes: *Staphylococcus aureus*(methicillin-susceptible)* *Coagulase negative taphylococcus*(methicillin susceptible) *Streptococcus pyogenes* *Streptococcus agalactiae*
Gram-negative aeobes: *Haemophilus influenzae Haemophilus parainfluenzae Moraxella catarrhalis* Spirochaetes: *Borrelia burgdorferi*
Microorganisms for which acquired resistance may be a problem
Gram-positive aeobes: *Streptococcus pneumoniae*
Gram-negative aeobes: *Citrobacter freundii* *Enterobacter aerogenes* *Enterobacter cloacae* *Escherichia coli* *Klebsiella pneumoniae* *Proteus mirabilis* *Proteus*spp. (other than*P. vulgaris)* *Providencia* spp.
Gram-positive anaeobes: *Peptostreptococcus* spp. *Propionibacterium* spp.
Gram-negative anaeobes: *Fusobacterium* spp. *Bacteroides* spp.
Inherently resistant microorganisms
Gram-positive aeobes: *Enterococcus faecalis Enterococcus faecium*
Gram-negative aeobes: *Acinetobacter* spp. *Campylobacter* spp. *Morganella morganii Proteus vulgaris Pseudomonas aeruginosa* *Serratia marcescens* Gram-negative anaeobes: *Bacteroides fragilis* Others: *Chlamydia* spp. *Mycoplasma* spp. *Legionella* spp.

* All methicillin-resistant *S. aureus* are resistant to cefuroxime.

Pharmacokineticprroperties Absorption
Afer oral administrratiocefuroxime axaxetis absorbed from the gastrointestestitract and rapidly hydrolysed in the intesntestmucosa and blood to release cefuroxime into the cire circulation.
Optimum absorptiooccurs when it is administered shortly y er a meal.
Following administrationof cefuroxime axxetitablets peak serum levels (2.9 µg/mL for a 125 mg dose, 4.4 µg/mL for a 250 mg dose, 7.7 µg/mL for a 500 mg dose and 13.6 µg/mL for a 1000 mg dose) occur approximately 2.4 hours afer dosing when taken with food. The pharmacokineticof cefuroxime is linear over the oral dosage range of 125 to 1000 mg. No o accumulatiof cefuroxime occurred following repeat oral doses of 250 to 500 mg.
Distribution
Protein binding has been stated as 33 to 50% depending on the methodology used. Following a single dose of cefuroxime axetil500 mg tablet to 12 healthy volunteers, the apparent volume of distributionwas 50 L (CV%=28%). Concentrrationof cefuroxime in excess of the minimum inhibitory levels for common pathogens can be achieved in the tonsilla, sinus s tissuebronchial mucosa, bone, pleural fluid, joint fluid, synovial fluid, interserstifluid, bile, sputum and aqueous humor. Cefuroxime passes the blood-brain barrier when the meninges are inflamed.
Biotransformation
Cefuroxime is not metabolised.
Elimination
The serum half-life is between 1 and 1.5 hours. Cefuroxime is excreted by glomerular filtrratioand tubular secrcretioThe renal clearance is in the region of 125 to 148 mL/min/1.73 m^2.
Special patient populations Gender
No differences in the pharmacokineticof cefuroxime were observed between males and females.
Elderly
No special precautionis necessary in the elderly patientwith normal renal l functiat dosages up to the normal maximum of 1 g per day. Elderly ly patieare more likely to have decreased renal function;therefore, the dose should be adjusted in accordance with the renal functioin the elderly.
Paediatric population
In older infants (aged >3 months) and in children, the pharmacokineticsof cefuroxime are similar to that observed in adults.
There is no clinical trial data available on the use of cefuroxime axetilin children under the age of 3 months.
Renal impairment
The safety and efficacy of cefuroxime axaxetin in patiewith renal failure have not been established.
Cefuroxime is primarily excreted by the kidneys. Therefore, as with all such antibioticsin n patienwith markedly impaired renal al funct(i.e. C1cr <30 mL/minute) it is recommended that the dosage of cefuroxime should be reduced to compensate for its slower excretion.Cefuroxime is effffecely removed by dialysis.
Hepaticimpairment
There are no data available for patientswith hepatiimpairment. Since cefuroxime is primarily eliminated by the kidney, the presence of f hepatic dysfunctis expected to have no effect on the pharmacokineticsof cefuroxime.
PK/PD relationship
For cephalosporins, the most important pharmacokinetic-pharmacodynamicindex corrrelatinwith *in vivo* efficacy has been shown to be the percentage of the dosing interval (%T) that the unbound concentrationremains above the minimum inhibitory concentrratio(MIC) of cefuroxime for individual target species (i.e. %T>MIC).

INCOMPATIBILITY Not applicable.

SHELF LIFE Refer on carton

STORAGE INSTRUCTIONS
Store protected from light & moisture, at a temperature not exceeding 30°C.

PACKAGING INFORMATION 10x10 Tablets
Keep all medicines out of reach of children.

Manufactured by : Malik Lifesciences Pvt. Ltd.
(A subsidiary of Akums Drugs & Pharmaceuticals Ltd.) Plot No.16, Vardhman Indl. Estate, Vill-Bahadarpur Saini, N.H. 58, Haridwar-247 667, (Uttarakhand)
Marketed by:
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