ZINEX

Tablets

Composition
Each tablet contains Cefuroxime (as axetil) 250 or 500 mg

Action
Cefuroxime axetil owes its bactericidal activity to the parent compound cefuroxime. Cefuroxime is a well-characterized and effective antibacterial agent that has bactericidal activity against a wide range of common pathogens, including β-lactamase producing strains.

Cefuroxime has good stability to bacterial β-lactamase, and consequently is active against many ampicillin-resistant or amoxycillin-resistant strains. The bactericidal action of cefuroxime results from inhibition of cell wall synthesis by binding to essential target proteins.

Cefuroxime is usually active against the following organisms:

Aerobes Gram-negative

- *Haemophilus influenzae (including ampicillin-resistant strains)*
- *Haemophilus parainfluenzae*
- *Moraxella (Branhamella) catarrhalis*
- *Neisseria gonorrhoeae (including penicillinase and non- penicillinase producing strains)*
- *Escherichia coli*
- *Klebsiella spp.*
- *Proteus mirabilis*
- *Providencia spp.*
- *Proteus rettgeri.*

Aerobes Gram-positive

- *Staphylococcus aureus* and *Staphylococcus epidermidis* (including penicillinase producing strains but excluding methicillin resistant strains)
- *Streptococcus pyogenes* (and other β-haemolytic streptococci)
- *Streptococcus pneumoniae*
- Streptococcus Group B (Streptococcus agalactiae)

Anaerobes

- Gram-positive and Gram-negative cocci (including Peptococcus and Peptostreptococcus species)
- Gram-positive bacilli (including Clostridium species) and Gram- negative bacilli (including Bacteroides and Fusobacterium species)
- Propionibacterium spp.

Other organisms

- *Borrelia burgdorferi*

The following organisms are not susceptible to Cefuroxime:-

- *Clostridium difficile*
- *Pseudomonas spp.*
- *Campylobacter spp.*
- *Acinetobacter calcoaceticus*
- *Listeria monocytogenes*
- Methicillin resistant strains of Staphylococcus aureus and Staphylococcus epidermidis.
- *Legionella spp.*

Some strains of the following genera are not susceptible to Cefuroxime:-

- Enterococcus (Streptococcus) faecalis
- *Morganella morganii*
- *Proteus vulgaris*

- Enterobacter spp.
- Citrobacter spp.
- Serratia spp.
- *Bacteroides fragilis.*

Pharmacokinetics

Absorption

After oral administration cefuroxime axetil is absorbed from the gastrointestinal tract and rapidly hydrolysed in the intestinal mucosa and blood to release cefuroxime into the circulation. Optimum absorption occurs when it is administered shortly after a meal.

Following administration of cefuroxime axetil tablets 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 after dosing when taken with food. The rate of absorption of cefuroxime from the suspension is reduced compared with the tablets, leading to later, lower peak serum levels and reduced systemic bioavailability (4 to 17% less). Cefuroxime axetil oral suspension was not bioequivalent to cefuroxime axetil tablets when tested in healthy adults and therefore is not substitutable on a milligram-per-milligram basis .The pharmacokinetics of cefuroxime is linear over the oral dosage range of 125 to 1000 mg. No accumulation of 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 axetil 500 mg tablet to 12 healthy volunteers, the apparent volume of distribution was 50 L (CV%=28%). Concentrations of cefuroxime in excess of the minimum inhibitory levels for common pathogens can be achieved in the tonsilla, sinus tissues, bronchial mucosa, bone, pleural fluid, joint fluid, synovial fluid, interstitial fluid, 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 filtration and tubular secretion. The renal clearance is in the region of 125 to 148 mL/min/1.73 m^2.

Special patient populations

Gender

No differences in the pharmacokinetics of cefuroxime were observed between males and females.

Elderly

No special precaution is necessary in the elderly patients with normal renal function at dosages up to the normal maximum of 1 g per day. Elderly patients are more likely to have decreased renal function; therefore, the dose should be adjusted in accordance with the renal function in the elderly.

Paediatrics

In older infants (aged >3 months) and in children, the pharmacokinetics of cefuroxime are similar to that observed in adults.

There is no clinical trial data available on the use of cefuroxime axetil in children under the age of 3 months.

Renal impairment

The safety and efficacy of cefuroxime axetil in patients with renal failure have not been established. Cefuroxime is primarily excreted by the kidneys. Therefore, as with all such antibiotics, in patients with markedly impaired renal function (i.e. C1cr <30 mL/minute) it is recommended that the dosage

of cefuroxime should be reduced to compensate for its slower excretion (see section 4.2). Cefuroxime is effectively removed by dialysis.

Hepatic impairment
There are no data available for patients with hepatic impairment. Since cefuroxime is primarily eliminated by the kidney, the presence of hepatic dysfunction is expected to have no effect on the pharmacokinetics of cefuroxime.

Indications
Zinex is indicated for the treatment of infections caused by susceptible strains of the following organisms in the following infections:

- Pharyngitis and tonsillitis caused by *Streptococcus pyogenes*.
- Otitis media caused by *Streptococcus pneumoniae, Haemophilus influenza* (ampicillin- sensitive and resistant strains), *Moraxella (Branhamella) catarrhalis* and *Streptococcus pyogenes.*
- Sinusitis caused by *Streptococcus pneumoniae* and *Haemophilus influenza*.
- Acute and chronic bronchitis caused by *Streptococcus pneumoniae*, *Haemophilus influenza* (ampicillin-sensitive strains) and *Haemophilus parainfluenzae* (ampicillin-sensitive strains).
- Acute uncomplicated cystitis caused by *Escherichia coli* and *Klebsiella pneumoniae.*
- Lyme disease caused by *Borrelia burgdorferi*.

Contraindications
- Hypersensitivity to cephalosporin antibiotics or to any components of the formulation.
- Hypersensitivity to penicillin and other beta-lactam antibiotics.

Warnings
Cefuroxime should be used with caution in patients with:

- A history of gastrointestinal disease, especially ulcerative colitis, regional enteritis or pseudomembranous colitis.
- Renal function impairment - A reduced dose may be required.
- Porphyria: Safety has not been established.

Pseudomembranous colitis may occur. Patients who develop abdominal or stomach cramps, abdominal tenderness, severe and watery diarrhea (which may be bloody) and fever, should be investigated for this diagnosis. If the diagnosis of pseudomembranous colitis is suspected, Cefuroxime should be stopped immediately and appropriate therapy initiated.

Adverse Reactions
Hematological: Eosinophilia

Neurological: Headache

Gastrointestinal: Nausea, vomiting, abdominal pain, diarrhea, in some cases accompanied by blood in stools, which may be a symptom of enterocolitis. A particular form of enterocolitis is pseudomembranous colitis .

Kidney/Genitourinary: Vaginal candidiasis

Liver: Transient increases in hepatic enzyme levels

Skin: Erythema multiforme, Stevens Johnson syndrome, toxic epidermal necrolysis

Other: Hypersensitivity reactions including skin rashes, urticaria, pruritus, bronchospasm, drug fever, serum sickness, and anaphylaxis

Precautions

Prolonged use of Cefuroxime may result in the overgrowth of non-susceptible organisms (e.g. Candida, Enterococci, or Clostridium difficile).
Pseudomembranous colitis has been reported with the use of Cefuroxime. Patients who develop abdominal or stomach cramps, abdominal tenderness, severe and watery diarrhea (which may be bloody) and fever should be investigated for this diagnosis.
The Jarisch-Herxheimer reaction has been reported following treatment with Cefuroxime for Lyme disease. This reaction is a common and usually self-limiting consequence of antibiotic treatment for Lyme disease.

Pregnancy
Category B
Animal reproduction studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies in pregnant women.

Nursing Mothers
Cefuroxime is excreted in human milk, and consequently caution should be exercised when cefuroxime axetil is administered to a nursing mother.

Drug Interactions
Concurrent administration of probenecid increases the area under the mean serum concentration time-curve by 50%.

Diagnostic Interference
It is recommended that glucose either oxidase or hexokinase methods be used to determine blood/plasma glucose levels in patients receiving Cefuroxime.
This medicine may give false-negative test results with ferricyanide blood glucose test. Cefuroxime does not interfere in the alkaline picrate assay for creatinine.
A false-positive Coombs reaction may appear in patients who receive large doses of Cefuroxime.

Dosage and Administration
Adults
Sinusitis & acute or chronic bronchitis
250 mg twice daily for seven days (Range 5-10 days)

Acute - uncomplicated cystitis
125 mg twice daily for seven days (Range 5-10 days)

Lyme disease
Adults and children over 12 years of age: 500 mg twice daily for 20 days

Children
There is no experience with Zinex in children under 3 months of age.
3 months to 2 years of age: 125 mg twice daily
Over 2 years of age: 250 mg twice daily

Zinex should be taken half an hour after food for optimum absorption.

Over Dosage
Overdosage of cephalosporins can cause cerebral irritation leading to convulsions.

Serum levels of cefuroxime can be reduced by haemodialysis or peritoneal dialysis.

Presentation
Zinex 250
Box of 10 tablets

Zinex 500
Box of 10 tablets