Cefuroxime axetil

Zinnat® Tablets

PRODUCT DESCRIPTION

Cefuroxime (as axetil) *(Zinnat®)* 250mg tablet:.
Each white, film-coated, capsule-shaped tablet engraved with 'GXES7' on one side tablet contains 250mg of Cefuroxime (as axetil).
Cefuroxime (as axetil) *(Zinnat®)* 500mg tablet:
Each white, film-coated, capsule-shaped tablet engraved with 'GXEG2' on one side tablet contains 500mg of Cefuroxime (as axetil).

PHARMACOLOGIC PROPERTIES

Pharmacodynamics
The prevalence of acquired resistance is geographically and time dependent and for select species may be very high. Local information on resistance is desirable, particularly when treating severe infections.

In vitro susceptibility of micro-organisms to Cefuroxime Where clinical efficacy of cefuroxime axetil has been demonstrated in clinical trials this is indicated with an asterisk (*).
Commonly Susceptible Species
Gram-Positive Aerobes: *Staphylococcus aureus (methicillin susceptible)** *Coagulase negative staphylococcus (methicillin susceptible)* *Streptococcus pyogenes** *Beta-hemolytic streptococci*
Gram-Negative Aerobes: *Haemophilus influenzae* including ampicillin resistant strains* *Haemophilus parainfluenzae** *Moraxella catarrhalis** *Neisseria gonorrhoea* including penicillinase and non-penicillinase producing strains*
Gram-Positive Anaerobes: *Peptostreptococcus spp.* *Propionibacterium spp.*
Spirochetes: *Borrelia burgdorferi**
Organisms for which acquired resistance may be a problem
Gram-Positive Aerobes: *Streptococcus pneumoniae**
Gram-Negative Aerobes: *Citrobacter spp. not including C. freundii* *Enterobacter spp. not including E. aerogenes and E. cloacae* *Escherichia coli** *Klebsiella spp. including Klebsiella pneumoniae** *Proteus mirabilis* *Proteus spp. not including P. penneri and P. vulgaris* *Providencia spp.*
Gram-Positive Anaerobes: *Clostridium spp. not including C. difficile*
Gram-Negative Anaerobes: *Bacteroides spp. not including B. fragilis* *Fusobacterium spp.*
Inherently resistant organisms
Gram-Positive Aerobes: *Enterococcus spp. including E. faecalis and E. faecium*

Listeria monocytogenes
Gram-Negative Aerobes:
Acinetobacter spp.
Burkholderia cepacia
Campylobacter spp.
Citrobacter freundii
Enterobacter aerogenes
Enterobacter cloacae
Morganella morganii
Proteus penneri
Proteus vulgaris
Pseudomonas spp. including Pseudomonas aeruginosa
Serratia spp.
Stenotrophomonas maltophilia
Gram-Positive Anaerobes:
Clostridium difficile
Gram-Negative Anaerobes:
Bacteroides fragilis
Others:
Chlamydia species
Mycoplasma species
Legionella species

Pharmacokinetics
Absorption
After oral administration Cefuroxime (as axetil) *(Zinnat®)* is slowly 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 (as axetil) *(Zinnat®)* tablets peak serum levels (2.1mg/l for a 125mg dose, 4.1mg/l for a 250mg dose, 7.0mg/l for a 500mg dose and 13.6mg/l for a 1g dose) occur approximately 2 to 3 hours after dosing when taken with food.
Distribution
Protein binding has been variously stated as 33 to 50% depending on the methodology used.
Metabolism
Cefuroxime is not metabolized.
Elimination
The serum half life is between 1 and 1.5 hours.
Cefuroxime is excreted by glomerular filtration and tubular secretion. Concurrent administration of probenecid increases the area under the mean serum concentrations time curve by 50%.
Renal impairment
Cefuroxime pharmacokinetics have been investigated in patients with various degrees of renal impairment. Cefuroxime elimination half-life increases with decrease in renal function which serves as the basis for dosage adjustment recommendations in this group of patients (*See Dosage and Administration*). In patients undergoing haemodialysis, at least 60% of the total amount of cefuroxime present in the body at the start of dialysis will be removed during a 4-hour dialysis period. Therefore, an additional single dose of cefuroxime should be administered following the completion of haemodialysis.
Pre-clinical Safety Data
Animal toxicity studies indicated that cefuroxime axetil is of low toxicity with no significant findings.

INDICATIONS
Cefuroxime (as axetil) *(Zinnat®)* is an oral prodrug of the bactericidal cephalosporin antibiotic cefuroxime, which is resistant to most β (beta) -lactamases and is active against a wide range of Gram-positive and Gram-negative organisms.
It is indicated for the treatment of infections caused by susceptible bacteria.
Susceptibility to Cefuroxime (as axetil) *(Zinnat®)* will vary with geography and time and local susceptibility data should be consulted where available *(See Pharmacological properties, Pharmacodynamics).*

Indications include:
- upper respiratory tract infections for example, ear, nose and throat infections, such as otitis media, sinusitis, tonsillitis and pharyngitis
- lower respiratory tract infections for example, pneumonia, acute bronchitis, and acute exacerbations of chronic bronchitis
- genito-urinary tract infections for example, pyelonephritis, cystitis and urethritis
- skin and soft tissue infections for example, furunculosis, pyoderma and impetigo
- gonorrhoea, acute uncomplicated gonococcal urethritis, and cervicitis.
- treatment of early Lyme disease and subsequent prevention of late Lyme disease in adults and children over 12 years old.

Cefuroxime is also available as the sodium salt (*Zinacef®*) for parenteral administration. This permits the use of sequential therapy with the same antibiotic, when a change from parenteral to oral therapy is clinically indicated.
Where appropriate Cefuroxime (as axetil) *(Zinnat®)* is effective when used following initial parenteral cefuroxime sodium (*Zinacef®)* in the treatment of pneumonia and acute exacerbations of chronic bronchitis.

DOSAGE AND ADMINISTRATION

The usual course of therapy is seven days (range 5 to 10 days).
Cefuroxime (as axetil) *(Zinnat®)* should be taken after food for optimum absorption.

- **Adults**

Most infections	250mg twice daily
Urinary tract infections	125mg twice daily
Mild to moderate lower respiratory tract infections e.g. bronchitis	250mg twice daily
More severe lower respiratory tract infections, or if pneumonia is suspected	500mg twice daily
Pyelonephritis	250mg twice daily
Uncomplicated gonorrhoea	single dose of 1g
Lyme disease in adults and children over the age of 12 years	500mg twice daily for 20 days

Sequential therapy

Pneumonia

1.5g Cefuroxime sodium *(Zinacef®)* three times a day or twice a day (intravenous (i.v.) or intramuscular (i.m.)) for 48 to 72 hours, followed by Cefuroxime (as axetil) *(Zinnat®)* oral therapy 500mg twice a day for 7 to10 days.

Acute exacerbations of chronic bronchitis

750 mg Cefuroxime sodium *(Zinacef®)* three times a day or twice a day (i.v. or i.m.) for 48 to 72 hours, followed by Cefuroxime (as axetil) *(Zinnat®)* oral therapy 500mg twice a day for 5 to 10 days.

Duration of both parenteral and oral therapy is determined by the severity of the infection and the clinical status of the patient.

- **Children**

Most infections	125mg (1 x 125mg tablet) twice daily, to a maximum of 250mg daily.
Children aged two years or older with otitis media or, where appropriate, with more severe infections	250mg (1 x 250mg tablet or 2 x 125mg tablets) twice daily, to a maximum of 500mg daily.

Cefuroxime (as axetil) *(Zinnat®)* tablets should not be crushed and are therefore unsuitable for treatment of patients, such as younger children, who cannot swallow tablets. In children Cefuroxime (as axetil) *(Zinnat®)* oral suspension may be used.
There is no experience of using Cefuroxime (as axetil) *(Zinnat®)* in children under the age of 3 months.

- **Renal impairment**

Cefuroxime is primarily excreted by the kidneys. In patients with markedly impaired renal function it is recommended that the dosage of cefuroxime be reduced to compensate for its slower excretion (see the table below).

Creatinine Clearance	$T_{1/2}$ (hours)	Recommended Dosage
≥30 ml/min	1.4 - 2.4	No dose adjustment necessary standard dose of 125 mg to 500 mg given twice daily
10-29 ml/min	4.6	Standard individual dose given every 24 hours
<10 ml/min	16.8	Standard individual dose given every 48 hours
During haemodialysis	2 – 4	A single additional standard individual dose should be given at the end of each dialysis

CONTRAINDICATIONS

Patients with known hypersensitivity to cephalosporin antibiotics.

WARNINGS & PRECAUTIONS

Special care is indicated in patients who have experienced an allergic reaction to penicillins or other beta-lactams.
As with other antibiotics, use of Cefuroxime (as axetil) *(Zinnat®)* may result in the overgrowth of Candida. Prolonged use may also result in the overgrowth of other non-susceptible organisms (e.g. enterococci and Clostridium difficile), which may require interruption of treatment.
Pseudomembranous colitis has been reported with the use of antibiotics, and may range in severity from mild to life-threatening. Therefore, it is important to consider its diagnosis in patients who develop diarrhoea during or after antibiotic use. If prolonged or significant diarrhoea occurs or the patient experiences abdominal cramps, treatment should be discontinued immediately and the patient investigated further.

The Jarisch-Herxheimer reaction has been seen following Cefuroxime (as axetil) *(Zinnat®)* treatment of Lyme disease. It results directly from the bactericidal activity of Cefuroxime (as axetil) *(Zinnat®)* on the causative organism of Lyme disease, the spirochaete *Borrelia burgdorferi*. Patients should be reassured that this is a common and usually self-limiting consequence of antibiotic treatment of Lyme disease.
With a sequential therapy regime the timing of change to oral therapy is determined by severity of the infection, clinical status of the patient and susceptibility of the pathogens involved. If there is no clinical improvement within 72 hours, then the parenteral course of treatment must be continued.
Please refer to the relevant prescribing information for cefuroxime sodium before initiating sequential therapy.

Ability to perform tasks that require judgement, motor or cognitive skills

As this medicine may cause dizziness, patients should be warned to be cautious when driving or operating machinery.

DRUG INTERACTIONS

Drugs which reduce gastric acidity may result in a lower bioavailability of Cefuroxime (as axetil) *(Zinnat®)* compared with that of the fasting state and tend to cancel the effect of enhanced post-prandial absorption.

In common with other antibiotics, Cefuroxime (as axetil) *(Zinnat®)* may affect the gut flora, leading to lower oestrogen reabsorption and reduced efficacy of combined oral contraceptives.
As a false negative 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 patients receiving Cefuroxime (as axetil) *(Zinnat®)*. This antibiotic does not interfere in the alkaline picrate assay for creatinine.

PREGNANCY AND LACTATION

There is no experimental evidence of embryopathic or teratogenic effects attributable to cefuroxime axetil but, as with all drugs, it should be administered with caution during the early months of pregnancy. Cefuroxime is excreted in human milk, and consequently caution should be exercised when cefuroxime axetil is administered to a nursing mother.

ADVERSE EFFECTS

Adverse drug reactions to Cefuroxime (as axetil) *(Zinnat®)* are generally mild and transient in nature.
The frequency categories assigned to the adverse reactions below are estimates, as for most reactions suitable data (for example from placebo-controlled studies) for calculating incidence were no t available. In addition the incidence of adverse reactions associated with Cefuroxime (as axetil) *(Zinnat®)* may vary according to the 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-marketing data and refer to a reporting rate 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 (investigator assessed) data.
The following convention has been used for the classification of frequency:

very common ≥1/10
common ≥1/100 to <1/10
uncommon ≥1/1000 to <1/100
rare ≥1/10,000 to <1/1000
very rare <1/10,000

Infections and infestations
Common: Overgrowth of Candida
Blood and lymphatic system disorders
Common: *Eosinophilia
Uncommon: *Positive Coombs' test, *thrombocytopenia, *leukopenia (sometimes profound)
Very rare: *Haemolytic anaemia
Cephalosporins as a class tend to be absorbed onto the surface of red cells membranes and react with antibodies directed against the drug to produce a positive Coombs' test (which can interfere with cross-matching of blood) and very rarely haemolytic anaemia.
Immune system disorders
***Hypersensitivity reactions including**
Uncommon: *Skin rashes
Rare: *Urticaria, *pruritus
Very rare: *Drug fever, *serum sickness, *anaphylaxis
Nervous system disorders
Common: *Headache, dizziness
Gastrointestinal disorders
Common: *Gastrointestinal disturbances including *diarrhoea, *nausea, abdominal pain
Uncommon: *Vomiting
Rare: *Pseudomembranous colitis *(See Warnings and Precautions)*
Hepatobiliary disorders
Common: *Transient increases of hepatic enzyme levels, [ALT (SGPT), AST (SGOT), LDH]
Very rare: *Jaundice (predominantly cholestatic), *hepatitis
Skin and subcutaneous tissue disorders
Very rare: *Erythema multiforme, *Stevens-Johnson syndrome, *toxic epidermal necrolysis (exanthematic necrolysis)
See also Immune system disorders.

OVERDOSAGE

Signs and symptoms
Overdosage of cephalosporins can cause cerebral irritation leading to convulsions.
Treatment
Serum levels of cefuroxime can be reduced by haemodialysis and peritoneal dialysis.

STORAGE CONDITION

Cefuroxime (as axetil) *(Zinnat®) tablets* should be stored at temperatures not exceeding 30°C.
Protect from light.

AVAILABILITY

Cefuroxime (as axetil) *(Zinnat®) 250mg tablet:* 10 tablets per double-foil blister (box of 50's).
Cefuroxime (as axetil) *(Zinnat®) 500mg tablet:* 10 tablets per double-foil blister (box of 50's).

CAUTION

Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.
Keep all medicines out of reach of children.

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GlaxoSmithKline

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