Zinnat™ Tablets

Cefuroxime axetil

To the Medical and Pharmaceutical Professions.

Presentations

125 mg tablet - engraved GXES5 on one side and plain on the other. Each tablet contains cefuroxime 125 mg (as cefuroxime axetil).
250 mg tablet - engraved GXES7 on one side and plain on the other. Each tablet contains cefuroxime 250 mg (as cefuroxime axetil).
500 mg tablet - engraved GXEG2 on one side and plain on the other. Each tablet contains cefuroxime 500 mg (as cefuroxime axetil).

Indications

Cefuroxime axetil is an oral prodrug of the bactericidal cephalosporin antibiotic cefuroxime, which is resistant to most ß-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 sensitive bacteria.

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 Zinnat is effective when used following initial parenteral Zinacef (cefuroxime sodium) in the treatment of pneumonia and acute exacerbations of chronic bronchitis.

Dosage and Administration

The usual course of therapy is seven days.
Cefuroxime axetil should be taken after food for optimum absorption.

Dosage in adults:

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

Sequential therapy:

Pneumonia:
1.5 g Zinacef bd (IV or IM) for 48-72 hours, followed by 500 mg bd Zinnat (cefuroxime axetil) oral therapy for 7 days.
Acute exacerbations of chronic bronchitis:
750 mg Zinacef bd (IV or IM) for 48-72 hours, followed by 500 mg bd Zinnat (cefuroxime axetil) oral therapy for 5-7 days.
Duration of both parenteral and oral therapy is determined by the severity of the infection and the clinical status of the patient.

Dosage in children:

Most infections	125 mg twice daily or 10mg/kg bd, to a maximum of 250 mg daily.
Children aged two years or older with otitis media or, where appropriate, with more severe infections	250 mg twice daily or 15mg/kg bd, to a maximum of 500 mg daily.

For otitis media, in children less than 2 years of age the usual dosage is 125mg bd or 10mg/kg bd to a maximum of 250mg daily.
Zinnat tablets should not be crushed and are therefore unsuitable for treatment of patients, such as younger children, who cannot swallow tablets. In children Zinnat oral suspension may be used.
There is no experience of using Zinnat in children under the age of 3 months.
Zinnat Tablets should not be crushed, therefore in younger children the suspension is more appropriate.

Elderly and patients with renal impairment

No special precautions are necessary in patients with renal impairment or on renal dialysis or in the elderly at dosages up to the normal maximum of 1g per day.

Contra-indications

Patients with known hypersensitivity to cephalosporin antibiotics.

Precautions and Warnings

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 axetil 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 broad- spectrum antibiotics, therefore, it is important to consider its diagnosis in patients who develop serious diarrhoea during or after antibiotic use.
The Jarisch-Herxheimer reaction has been seen following Zinnat treatment of Lyme disease. It results directly from the bactericidal activity of 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.

Drug Interactions

In common with other antibiotics, 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 axetil. This antibiotic does not interfere in the alkaline picrate assay for creatinine.
A positive Coomb's test has been reported during treatment with cephalosporins. This phenomenon can interfere with cross matching of blood.

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 Reactions

Adverse drug reactions to cefuroxime axetil 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 not available. In addition the incidence of adverse reactions associated with cefuroxime axetil 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 and <1/10, *Uncommon* ≥ 1/1000 and <1/100, *Rare* ≥ 1/10,000 and <1/1000 and *Very rare* <1/10,000.

Infections and infestations
Common: Candida overgrowth from prolonged use
Blood and lymphatic system disorders
Common: Eosinophilia
Uncommon: Positive Coombs' test, thrombocytopenia, leukopenia (sometimes profound)
Very rare: 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
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)

Overdosage

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

Pharmacodynamic Properties

Bacteriology:
Cefuroxime axetil owes its *in vivo* bactericidal activity to the parent compound cefuroxime.
Cefuroxime is a well characterised and effective antibacterial agent which has bactericidal activity against a wide range of common pathogens, including ß-lactamase producing strains.
Cefuroxime has good stability to bacterial ß-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 *in vitro*.

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 ß-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.

Pharmacokinetic Properties

After oral administration cefuroxime axetil 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.
Peak serum cefuroxime levels occur approximately two to three hours after oral dosing. The serum half life is about 1.2 hours. Approximately 50% of serum cefuroxime is protein bound. Cefuroxime is not metabolised and is excreted by glomerular filtration and tubular secretion.
Concurrent administration of probenecid increases the area under the mean serum concentrations time curve by 50%.

Pharmaceutical Precautions and Recommendations

Do not store above 30°C.

List of Excipients

Microcrystalline cellulose
Croscarmellose sodium, Type A
Sodium lauryl sulphate
Hydrogenated vegetable oil
Silica Colloidal Anhydrous
Methylhydroxypropyl cellulose
Propylene glycol
Methyl parahydroxybenzoate
Propyl parahydroxybenzoate
Opaspray white M-1-7120J

THIS IS A MEDICAMENT

Medicament is a product which affects your health and its consumption contrary to instructions is dangerous for you.
Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.
- The doctor and the pharmacist are the experts in medicines, their benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed.
- Do not repeat the same prescription without consulting your doctor.
- **Keep all medicaments out of reach of children.**

Council of Arab Health Ministers
Union of Arab Pharmacists

GlaxoSmithKline

Packed by
Pharmaline - Lebanon
Licensed by
GlaxoSmithKline Export Limited, U.K.

Rev. 04/2010 905075-A

Not all strengths are registered in every market
Text version: GDS_V22
Date of issue: 04 January 2007

ZINNAT is a Trademark of the GlaxoSmithKline group of companies
© 2006 GlaxoSmithKline group of companies.
All rights reserved.