ZINNAT™ SUSPENSION

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Cefuroxime axetil

Presentation
Zinnat Suspension contains granules of cefuroxime axetil for oral suspension. Reconstitution of the multidose bottles as directed yields a suspension containing 125mg or 250mg of cefuroxime (as cefuroxime axetil) in each 5ml.

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:

Lower respiratory tract infections for example, acute bronchitis, acute exacerbations of chronic bronchitis and pneumonia.

Upper respiratory tract infections for example, ear, nose, throat infections, such as otitis media, sinusitis, tonsilitis and pharyngitis.

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.

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

Pharmacological Properties
Pharmacodynamic Properties:
Cefuroxime axetil is an oral prodrug of the bactericidal cephalosporin antibiotic cefuroxime, which is resistant to most beta-lactamases and is active against a wide range of gram-positive and gram-negative organisms.
Microbiology: Cefuroxime axetil owes its *in vivo* bactericidal activity to the parent compound, cefuroxime. Cefuroxime is a well-characterised and effective antibacterial agent which has broad-spectrum bactericidal activity against a wide range of common pathogens, including beta-lactamase producing strains. Cefuroxime has good stability to bacterial beta-lactamase and consequently, is active against many ampicillin-resistant strains and 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 catarrhalis, Escherichia coli, Klebsiella* species, *Proteus mirabilis, Proteus inconstans, Providencia* species, *Proteus rettgeri* and *Neisseria gonorrhoea* (including penicillinase and non-penicillinase producing strains).
Some strains of Morganella morganii, Enterobacter species and Citrobacter species have been shown by *in vitro* tests to be resistant to cefuroxime and other beta-lactam antibiotics.

Aerobes, Gram-positive: *Staphylococcus aureus* and *Staphylococcus epidermidis* (including penicillinase-producing strains but excluding methicillin-resistant strains), *Streptococcus pneumoniae* (and other beta-haemolytic streptococci), *Streptococcus Group B* (Streptococcus agalactiae) and *Propionibacterium* species.
Certain strains of enterococci, eg. Streptococcus faecalis, are resistant.

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). Most strains of Bacteroides fragilis are resistant.
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, Legionella spp.* and *Staphylococcus epidermidis.*

Some strains of the following genera are not susceptible to Cefuroxime: *Enterococcus faecalis, Morganella morganii, Proteus vulgaris, Enterobacter* spp., *Citrobacter* spp., *Serratia* spp., *Bacteroides fragilis.*

Pharmacokinetic Properties
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 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 concentration time curve by 50%. Serum levels of cefuroxime are reduced by dialysis.

Dosage and administration

Adults: Most infections will respond to 250mg b.d. In mild to moderate lower respiratory tract infections e.g. bronchitis 250mg b.d. should be given. For more severe lower respiratory tract infections, or if pneumonia is suspected then 500mg b.d. should be given. For urinary tract infections a dose of 125mg b.d. is usually adequate; in pyelonephritis the recommended dose is 250mg b.d. A single dose of one gram is recommended for the treatment of uncomplicated gonorrhoea.
Lyme disease in adults and children over the age of 12 years: the recommended dose is 500mg b.d. for 20 days.
Sequential therapy:
Pneumonia: 1.5g Zinacef bd (iv or im) for 48-72 hours, followed by 500mg bd Zinnat oral therapy for 7 days.
Acute exacerbations of chronic bronchitis: 750mg Zinacef bd (iv or im) for 48-72 hours, followed by 500mg Zinnat 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.
Children: The usual dose is 125mg b.d. (1 x 125mg tablet or 5ml of suspension), or 10mg/kg b.d. to a maximum of 250mg daily. For otitis media, in children less than 2 years of age the usual dosage is 125mg b.d. (1 x 125mg tablet or 5ml of suspension), or 10mg/kg b.d. to a maximum of 250mg daily and in children over 2 years of age, 250mg b.d. (1 x 250mg tablet or 10ml of suspension), or 15mg/kg b.d. to a maximum of 500mg daily. There is no experience in children under 3 months of age.
Zinnat Tablets should not be crushed, therefore in younger children the suspension is more appropriate.

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

Contra-indications
Hypersensitivity to cephalosporin antibiotics.

Special warnings and precautions for use:
Special care is indicated in patients who have experienced an anaphylactic reaction to penicillins or other beta-lactams.

As with other antibiotics, prolonged 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 diarrhoea during or after antibiotic use.

The sucrose content of Zinnat suspension and granules should be taken into account when treating diabetic patients, and appropriate advice provided. The Jarisch-Herxheimer reaction has been seen following Zinnat treatment of Lyme disease. 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 has been no clinical improvement after 72 hours of parenteral treatment, then the patient's treatment should be reviewed.

Zinnat suspension contains aspartame and should be used with caution in patients with phenylketonuria.

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.

Interactions:
Drugs which reduce gastric acidity may result in lower bioavailability of Zinnat.

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.

Adverse Reactions:
Adverse drug reactions to cefuroxime axetil are generally mild and transient in nature.
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
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
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 irritancy leading to convulsions.
Serum levels of cefuroxime can be reduced by haemodialysis or peritoneal dialysis.

List of Excipients:
Aspartame
Xanthan gum
Acesulfame potassium
Povidone K30
Stearic Acid
Sucrose
Tutti Frutti Flavour
Purified Water

Pharmaceutical precautions:
Zinnat Suspension granules should be stored below 30°C.
The reconstituted suspension must be refrigerated immediately at between 2 and 8°C.

The reconstituted suspension when refrigerated between 2°C and 8°C can be kept for up to 10 days.
Further diluted suspension from multidose bottles in cold fruit juices, or milk drinks should be taken immediately.
The reconstituted suspension should not be mixed with hot liquids.
Always shake the bottle vigorously before taking the medication.

Directions for reconstituting suspension in multidose bottles:-
1. Shake the bottle to loosen the granules.
2. Add the total amount of water to the bottle as stated on its label. Replace the cap.
3. Invert the bottle and rock vigorously at least 15 seconds.
4. Turn the bottle into an upright position and shake vigorously.
5. Refrigerate immediately at between 2 and 8°C.

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GlaxoSmithKline

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.