NEW ZEALAND
DATA SHEET

ZINNAT™
Cefuroxime axetil

Presentation

ZINNAT Tablets 250mg; white, film-coated, capsule-shaped tablets, 15mm long and 6.5mm wide, plain on one side and ‘GXES7’ on the other. Each tablet contains cefuroxime 250mg (as cefuroxime axetil).

Indications

Therapeutic indications

Cefuroxime axetil is an oral prodrug of the bactericidal cephalosporin antibiotic cefuroxime, which is resistant to most β-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. Susceptibility to cefuroxime axetil will vary with geography and time and local susceptibility data should be consulted where available (see Further Information).

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.

Skin and soft tissue infections for example, furunculosis, pyoderma and impetigo.

Gonorrhoea, acute uncomplicated gonococcal urethritis, and cervicitis.

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. (Range 5 - 10 days).

Cefuroxime axetil should be taken after food for optimum absorption.

**Adults**

Most infections

- 250mg twice daily

Mild to moderate lower respiratory tract infections e.g. bronchitis. Clinical evidence suggests a 5 day course of ZINNAT 250mg twice daily is as effective as a 10 day course for acute 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

**Sequential therapy:**

Pneumonia:-

1.5g ZINACEF three times daily or twice daily (iv or im) for 48-72 hours, followed by 500mg twice daily ZINNAT (cefuroxime axetil) oral therapy for 7-10 days.

Acute exacerbations of chronic bronchitis:-

750 mg ZINACEF three times daily or twice daily (iv or im) for 48-72 hours, followed by 500mg twice daily ZINNAT (cefuroxime axetil) oral therapy for 5-10 days.

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

**Children**

Children aged two years or older with otitis media or where appropriate with more severe infections 250mg (1 x 250mg tablet) twice daily, to a maximum of 500mg daily.
ZINNAT tablets should not be crushed and are therefore unsuitable for treatment of patients, such as younger children, who cannot swallow tablets.

There is no experience of using 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 ZINNAT be reduced to compensate for its slower excretion (see the table below).

<table>
<thead>
<tr>
<th>Creatinine Clearance</th>
<th>T1/2 (hours)</th>
<th>Recommended Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥30 mL/min</td>
<td>1.4 - 2.4</td>
<td>No dose adjustment necessary standard dose of 125 mg to 500 mg given twice daily</td>
</tr>
<tr>
<td>10-29 mL/min</td>
<td>4.6</td>
<td>Standard individual dose given every 24 hours</td>
</tr>
<tr>
<td>&lt;10 mL/min</td>
<td>16.8</td>
<td>Standard individual dose given every 48 hours</td>
</tr>
<tr>
<td>During haemodialysis</td>
<td>2 – 4</td>
<td>A single additional standard individual dose should be given at the end of each dialysis</td>
</tr>
</tbody>
</table>

**Contraindications**

Patients with known hypersensitivity to cephalosporin antibiotics.

**Warnings and 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 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 antibiotics and may range in severity from mild to life-threatening. Therefore, it is important to consider its diagnosis in patients who develop serious 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.

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.

**Use in Pregnancy**

There is no experimental evidence of embryopathic or teratogenic effects attributable to cefuroxime axetil but, as with all medicines, it should be administered with caution during the early months of pregnancy.

**Use and lactation**

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

**Effects on ability to drive and operate machinery**

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

---

**Adverse effects**

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 $\geq 1/10$
- common $\geq 1/100$ 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: 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 *(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.
Interactions

Medicines which reduce gastric acidity may result in a lower bioavailability of 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 axetil 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.

Overdose

Overdosage of cephalosporins can cause cerebral irritation leading to convulsions.

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

Further Information

Actions

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 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.

Pharmacodynamic properties

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 (*).

<table>
<thead>
<tr>
<th>Commonly Susceptible Species</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gram-Positive Aerobes:</strong></td>
</tr>
<tr>
<td>Staphylococcus aureus (methicillin susceptible)*</td>
</tr>
<tr>
<td>Coagulase negative staphylococcus (methicillin susceptible)</td>
</tr>
<tr>
<td>Streptococcus pyogenes*</td>
</tr>
<tr>
<td>Beta-hemolytic streptococci</td>
</tr>
<tr>
<td><strong>Gram-Negative Aerobes:</strong></td>
</tr>
<tr>
<td>Haemophilus influenzae* including ampicillin resistant strains</td>
</tr>
<tr>
<td>Haemophilus parainfluenzae*</td>
</tr>
<tr>
<td>Moraxella catarrhalis*</td>
</tr>
<tr>
<td>Neisseria gonorrhoea* including penicillinase and non-penicillinase producing strains</td>
</tr>
<tr>
<td><strong>Gram-Positive Anaerobes:</strong></td>
</tr>
<tr>
<td>Peptostreptococcus spp.</td>
</tr>
<tr>
<td>Propionibacterium spp.</td>
</tr>
<tr>
<td><strong>Spirochetes:</strong></td>
</tr>
<tr>
<td>Borrelia burgdorferi*</td>
</tr>
<tr>
<td>Organisms for which acquired resistance may be a problem</td>
</tr>
<tr>
<td><strong>Gram-Positive Aerobes:</strong></td>
</tr>
<tr>
<td>Streptococcus pneumoniae*</td>
</tr>
<tr>
<td><strong>Gram-Negative Aerobes:</strong></td>
</tr>
<tr>
<td>Citrobacter spp. not including C. freundii</td>
</tr>
<tr>
<td>Enterobacter spp. not including E. aerogenes and E. cloacae</td>
</tr>
<tr>
<td>Escherichia coli*</td>
</tr>
<tr>
<td>Klebsiella spp. including Klebsiella pneumoniae*</td>
</tr>
<tr>
<td>Proteus mirabilis</td>
</tr>
<tr>
<td>Proteus spp. not including P. penneri and P. vulgaris</td>
</tr>
<tr>
<td>Providencia spp.</td>
</tr>
<tr>
<td><strong>Gram-Positive Anaerobes:</strong></td>
</tr>
<tr>
<td>Clostridium spp. not including C. difficile</td>
</tr>
<tr>
<td><strong>Gram-Negative Anaerobes:</strong></td>
</tr>
<tr>
<td>Bacteroides spp. not including B. fragilis</td>
</tr>
<tr>
<td>Fusobacterium spp.</td>
</tr>
<tr>
<td>Inherently resistant organisms</td>
</tr>
<tr>
<td><strong>Gram-Positive Aerobes:</strong></td>
</tr>
<tr>
<td>Enterococcus spp. including E. faecalis and E. faecium</td>
</tr>
<tr>
<td>Listeria monocytogenes</td>
</tr>
</tbody>
</table>
**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 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 levels (4.1mg/L for a 250mg dose, 7.0mg/L for a 500mg dose and 13.6mg/L for a 1g dose) occur approximately two to three hours after dosing when taken after food.

Post peak levels, the serum half life is between 1 and 1.5 hours.

**Distribution**
Protein binding has been variously stated as 33-50% depending on the methodology used.

**Metabolism**
Cefuroxime is not metabolised.
Elimination

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.

Preclinical safety data

No additional data of relevance.

Excipients

Active ingredient
- Cefuroxime axetil.

List of excipients
- Microcrystalline cellulose.
- Croscarmellose Sodium.
- Hypromellose
- Sodium Lauryl Sulphate.
- Hydrogenated Vegetable oil.
- Silicon Dioxide.
- Propylene Glycol.
- Methylhydroxybenzoate (E218).
- Propylhydroxybenzoate (E216).
- Titanium Dioxide (E171).
- Sodium benzoate (E211).

Pharmaceutical Precautions

Incompatibilities

None reported.

Shelf life

Three years.
**Special precautions for storage**

ZINNAT tablets should be stored at temperatures not exceeding 30 °C.

**Package Quantities**

All strengths of tablets are supplied in cartons of 50, foil-wrapped.

**Medicines Schedule**

Prescription Only Medicine

**Sponsor Details**

GlaxoSmithKline NZ Ltd  
Private Bag 106600  
Downtown Auckland  
NEW ZEALAND

Phone: (09) 367 2900  
Facsimile: (09) 367 2506

**Date of preparation**

02 February 2015  
Version: 4.0

ZINNAT is a trade mark of the GSK group of companies.