ZINNAT Tablets  
Cefuroxime axetil

QUALITATIVE AND QUANTITATIVE COMPOSITION

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).

PHARMACEUTICAL FORM

Coated tablet.

CLINICAL PARTICULARS

Indications

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 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.

Dosage and Administration

The usual course of therapy is seven days (range 5 - 10 days).

ZINNAT should be taken after food for optimum absorption.
**Dosage in adults:**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most infections</td>
<td>250 mg twice daily</td>
</tr>
<tr>
<td>Urinary tract infections</td>
<td>250 mg twice daily</td>
</tr>
<tr>
<td>Mild to moderate lower respiratory tract infections e.g. bronchitis</td>
<td>250 mg twice daily</td>
</tr>
<tr>
<td>More severe lower respiratory tract infections, or if pneumonia is suspected</td>
<td>500 mg twice daily</td>
</tr>
<tr>
<td>Pyelonephritis</td>
<td>250 mg twice daily</td>
</tr>
<tr>
<td>Uncomplicated gonorrhoea</td>
<td>Single dose of 1 g</td>
</tr>
</tbody>
</table>

**Dosage in children:**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most infections</td>
<td>125 mg twice daily</td>
</tr>
<tr>
<td>Children with otitis media or, where appropriate, with more severe infections</td>
<td>250 mg (1 x 250 mg tablet) twice daily</td>
</tr>
</tbody>
</table>

*ZINNAT* tablets should not be crushed or split and are therefore unsuitable for treatment of patients, such as younger children, who cannot swallow whole tablets. When doses below 250 mg are required, *ZINNAT FOR SUSPENSION 125mg/5ml* should be used.

There is no experience of using *ZINNAT* in children under the age of 3 months.

**Dosage in 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).
<table>
<thead>
<tr>
<th>Creatinine Clearance</th>
<th>T$_{1/2}$ (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 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.

**Interactions**

Drugs 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 postprandial absorption.

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 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 ZINNAT 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 ZINNAT is administered to a nursing mother.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

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

Adverse Reactions

Adverse drug reactions to 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 not available. In addition, the incidence of adverse reactions associated with 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 $\geq 1/10$
- common $1/100$ to $<1/10$
- uncommon $1/1000$ to $<1/100$
- rare $1/10000$ to $<1/1000$
- very rare $<1/10000$

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*.

**Overdose**

**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.
PHARMACOLOGICAL 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-Negative Aerobes:

Haemophilus influenzae* including ampicillin-resistant strains
Haemophilus parainfluenzae*
Moraxella catarrhalis*
Neisseria gonorrhoeae* including penicillinase and non-penicillinase producing strains

Gram-Positive Aerobes:

Staphylococcus aureus (mecillin-susceptible)
Coagulase negative staphylococcus (mecillin-susceptible)
Streptococcus pyogenes*
Beta-hemolytic streptococci

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*

Methicillin-resistant strains of *Staphylococcus aureus* and *Staphylococcus* spp.

**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, 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 ZINNAT tablets, peak serum levels (2.1 mg/l for a 125 mg dose, 4.1 mg/l for a 250 mg dose, 7.0 mg/l for a 500 mg dose and 13.6 mg/l for a 1 g dose) occur approximately 2 to 3 hours after dosing when taken after food.

Distribution

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

Metabolism

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. 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.

Pharmaceutical particulars

Special precautions for storage

ZINNAT tablets should be stored below 25°C.
Not all presentations are available in every country.

Version number: GDS28/IPI08a(SI)
Date of issue: 14th September 2018

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Glaxo Wellcome Operations, UK

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