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).

CLINICAL INFORMATION
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 it should be used in accordance with local official antibiotic prescribing guidelines and local susceptibility data (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 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
Pharmaceutical Form: Coated tablet.
The usual course of therapy is seven days (range 5 - 10 days).
ZINNAT should be taken after food for optimum absorption.

Dosage in adults:

Indication	**Dosage**
Most infections	250 mg twice daily
Urinary tract infections	250 mg twice daily
Mild to moderate lower respiratory tract infections	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 1 g

Dosage in children:

Indication	**Dosage**
Most infections	125 mg twice daily
Children with otitis media or, where appropriate, with more severe infections	250 mg (1 x 250 mg tablet) twice daily

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. Therefore, *ZINNAT* suspension is recommended for patients 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).

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 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
Pregnancy
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.

Lactation
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 ≥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*.

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 (methicillin-susceptible)
Coagulase negative staphylococcus (methicillin-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.

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:
Clostridioides difficile

Gram-Negative Anaerobes:
Bacteroides fragilis

Others:
Chlamydia spp.
Mycoplasma spp.
Legionella spp.

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 INFORMATION

List of Excipients
Microcrystalline cellulose
Croscarmellose sodium, Type A
Methylhydroxypropylcellulose
Sodium lauryl sulphate
Hydrogenated vegetable oil
Silica Colloidal (anhydrous)
Propylene glycol
Methyl Parahydroxybenzoate
Propyl Parahydroxybenzoate
Titanium dioxide (E171)
Sodium benzoate

Shelf Life
The expiry date is indicated on the packaging.

Storage
The storage conditions are detailed on the packaging.
ZINNAT tablets should be stored below 25ºC.

Not all presentations are available in every country.

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