

NEW ZEALAND DATA SHEET

1. PRODUCT NAME

ZINNAT 250 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains cefuroxime 250 mg (as cefuroxime axetil).

Excipient with known effect

Sodium benzoate (E 211) and Propylene glycol.

For the full list of excipients, see section 6.1 List of excipients.

3. PHARMACEUTICAL FORM

White, film-coated, capsule-shaped tablets, 15 mm long and 6.5 mm wide, plain on one side and 'GXES7' on the other.

4. CLINICAL PARTICULARS

4.1 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.

ZINNAT is indicated in adults and children aged two years or older 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 section 5.1 Pharmacodynamic properties).

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.

4.2 Dose and method of administration

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

Dose

Adults

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

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.

Paediatric population

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.

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

Special populations

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).

Creatinine Clearance	T1/2 (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

Method of administration

ZINNAT tablets should be taken after food for optimum absorption.

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.

4.3 Contraindications

Patients with known hypersensitivity to cephalosporin antibiotics.

4.4 Special warnings and precautions for use

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.

4.5 Interaction with other medicines and other forms of interaction

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

4.6 Fertility, pregnancy and lactation

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.

Breast-feeding

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

Fertility

No data are available

4.7 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.

4.8 Undesirable effects

Summary of safety profile

Adverse drug reactions to cefuroxime axetil are generally mild and transient in nature.

Summary of adverse reactions

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 $\geq 1/1000$ to $< 1/100$

rare $\geq 1/10,000$ 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 section 4.4 Special warnings and precautions for use)

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.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected reactions via: <http://nzphvc.otago.ac.nz/reporting/>

4.9 Overdose

Overdosage of cephalosporins can cause cerebral irritation leading to convulsions.

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

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: antibacterials for systemic use, second-generation cephalosporins, ATC code: J01DC02

Mechanism of action

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 amoxicillin-resistant strains.

The bactericidal action of cefuroxime results from inhibition of cell wall synthesis by binding to essential target proteins.

Pharmacodynamic effects

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.

<p>In vitro susceptibility of micro-organisms to Cefuroxime</p> <p>Where clinical efficacy of cefuroxime axetil has been demonstrated in clinical trials this is indicated with an asterisk (*).</p>
<p>Commonly Susceptible Species</p>
<p><u>Gram-Positive Aerobes:</u></p> <p><i>Staphylococcus aureus (methicillin susceptible)*</i> <i>Coagulase negative staphylococcus (methicillin susceptible)</i> <i>Streptococcus pyogenes*</i> <i>Beta-hemolytic streptococci</i></p>
<p><u>Gram-Negative Aerobes:</u></p> <p><i>Haemophilus influenzae*</i> including ampicillin resistant strains <i>Haemophilus parainfluenzae*</i> <i>Moraxella catarrhalis*</i> <i>Neisseria gonorrhoea*</i> including penicillinase and non-penicillinase producing strains</p>
<p><u>Gram-Positive Anaerobes:</u></p> <p><i>Peptostreptococcus spp.</i> <i>Propionibacterium spp.</i></p>
<p><u>Spirochetes:</u></p> <p><i>Borrelia burgdorferi*</i></p>
<p>Organisms for which acquired resistance may be a problem</p>
<p><u>Gram-Positive Aerobes:</u></p> <p><i>Streptococcus pneumoniae*</i></p>
<p><u>Gram-Negative Aerobes:</u></p> <p><i>Citrobacter spp.</i> not including <i>C. freundii</i> <i>Enterobacter spp.</i> not including <i>E. aerogenes</i> and <i>E. cloacae</i> <i>Escherichia coli*</i> <i>Klebsiella spp.</i> including <i>Klebsiella pneumoniae*</i> <i>Proteus mirabilis</i> <i>Proteus spp.</i> not including <i>P. penneri</i> and <i>P. vulgaris</i> <i>Providencia spp.</i></p>
<p><u>Gram-Positive Anaerobes:</u></p> <p><i>Clostridium spp.</i> not including <i>C. difficile</i></p>
<p><u>Gram-Negative Anaerobes:</u></p> <p><i>Bacteroides spp.</i> not including <i>B. fragilis</i> <i>Fusobacterium spp.</i></p>
<p>Inherently resistant organisms</p>
<p><u>Gram-Positive Aerobes:</u></p> <p><i>Enterococcus spp.</i> including <i>E. faecalis</i> and <i>E. faecium</i> <i>Listeria monocytogenes</i></p>
<p><u>Gram-Negative Aerobes:</u></p> <p><i>Acinetobacter spp.</i> <i>Burkholderia cepacia</i> <i>Campylobacter spp.</i></p>

<i>Citrobacter freundii</i> <i>Enterobacter aerogenes</i> <i>Enterobacter cloacae</i> <i>Morganella morganii</i> <i>Proteus penneri</i> <i>Proteus vulgaris</i> <i>Pseudomonas</i> spp. including <i>Pseudomonas aeruginosa</i> <i>Serratia</i> spp. <i>Stenotrophomonas maltophilia</i>
<u>Gram-Positive Anaerobes:</u> <i>Clostridium difficile</i>
<u>Gram-Negative Anaerobes:</u> <i>Bacteroides fragilis</i>
<u>Others:</u> <i>Chlamydia</i> species <i>Mycoplasma</i> species <i>Legionella</i> species

5.2 Pharmacokinetic properties

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 (4.1 mg/L for a 250 mg dose, 7.0 mg/L for a 500 mg dose and 13.6 mg/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.

Biotransformation

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%.

Special populations

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 section 4.2 Dose and method of 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.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on studies of safety pharmacology, repeated dose toxicity, genotoxicity and toxicity to reproduction and development. No carcinogenicity studies have been performed; however, there is no evidence to suggest carcinogenic potential.

Gamma glutamyl transpeptidase activity in rat urine is inhibited by various cephalosporins, however the level of inhibition is less with cefuroxime. This may have significance in the interference in clinical laboratory tests in humans.

6. PHARMACEUTICAL PARTICULARS

6.1 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)

6.2 Incompatibilities

None reported.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

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

6.5 Nature and contents of container

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

6.6 Special precautions for disposal

There are no special requirements for disposal.

Any unused medicine should be disposed of in accordance with local requirements.

7. MEDICINE SCHEDULE

Prescription Medicine

8. SPONSOR

GlaxoSmithKline NZ Ltd
Private Bag 106600
Downtown Auckland
New Zealand

Phone: (09) 367 2900

Facsimile: (09) 367 2910

9. DATE OF FIRST APPROVAL

Date of publication in the New Zealand Gazette of consent to distribute the medicine:
15 December 1988

10. DATE OF REVISION OF THE TEXT

2 December 2020

Summary table of changes:

Section changed	Summary of new information
4.2	Clarification of method of administration

Version: 6.0

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