

# DATA SHEET

## ZINNAT™

### *Cefuroxime axetil*

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### Qualitative and quantitative composition

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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).

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### Pharmaceutical form

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Coated tablet.

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### Clinical particulars

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#### *Therapeutic indications*

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.

It is indicated for the treatment of infections caused by sensitive bacteria.

#### **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.

## ***Posology and method of 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.

### ***Contraindications***

Patients with known hypersensitivity to cephalosporin antibiotics.

### ***Special warnings and special 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 broad-spectrum antibiotics, therefore, it is important to consider its diagnosis in patients who develop serious diarrhoea during or after antibiotic use.

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.

### ***Interaction with other medicaments 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.

### ***Pregnancy and lactation***

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. 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***

None reported.

### ***Undesirable 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  $\geq 1/100$  and  $< 1/10$

uncommon  $\geq 1/1000$  and  $< 1/100$

rare  $\geq 1/10,000$  and  $< 1/1000$

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

#### Gastrointestinal disorders

Common: Gastrointestinal disturbances including diarrhoea, nausea

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)

See also Immune system disorders.

### **Overdose**

Overdosage of cephalosporins can cause cerebral irritation leading to convulsions.

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

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## **Pharmacological properties**

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### ***Pharmacodynamic properties***

#### **Bacteriology**

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  $\beta$ -lactamase producing strains.

Cefuroxime has good stability to bacterial  $\beta$ -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.

Cefuroxime is usually active against the following organisms *in vitro*.

#### **Aerobes Gram-negative**

Haemophilus influenzae (including ampicillin-resistant strains)

Haemophilus parainfluenzae

Moraxella (Branhamella) catarrhalis

Neisseria gonorrhoeae (including penicillinase and non- penicillinase producing strains)  
Escherichia coli  
Klebsiella spp.  
Proteus mirabilis  
Providencia spp.  
Proteus rettgeri.

**Aerobes Gram-positive**

Staphylococcus aureus and Staphylococcus epidermidis (including penicillinase producing strains but excluding methicillin resistant strains)  
Streptococcus pyogenes (and other  $\beta$  -haemolytic streptococci)  
Streptococcus pneumoniae  
Streptococcus Group B (Streptococcus agalactiae)

**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)  
Propionibacterium spp.

**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 and Staphylococcus epidermidis.  
Legionella spp.

Some strains of the following genera are not susceptible to Cefuroxime:-

Enterococcus (Streptococcus) faecalis  
Morganella morganii  
Proteus vulgaris  
Enterobacter spp.  
Citrobacter spp.  
Serratia spp.  
Bacteroides fragilis.

***Pharmacokinetic properties***

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 (4-6mg/L for a 250mg dose, 5-8mg/L for a 500mg dose and 9-14mg/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. Protein binding has been variously stated as 33-50% depending on the methodology used. Cefuroxime is not metabolised and is excreted by glomerular filtration and tubular secretion.

Concurrent administration of probenecid increases the area under the mean serum concentrations time curve by 50%.

Serum levels of cefuroxime are reduced by dialysis.

### ***Preclinical safety data***

No additional data of relevance.

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## **Pharmaceutical particulars**

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### ***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).

### ***Incompatibilities***

None reported.

### ***Shelf life***

Three years.

### ***Special precautions for storage***

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

### ***Nature and contents of container***

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

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## **Medicines classification**

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Prescription Only Medicine

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## **Name and address**

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## **Date of preparation**

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6 June 2007

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