Cefuroxime

QUALITATIVE AND QUANTITATIVE COMPOSITION
ZINNAT tablets containing either 125, 250 or 500 mg of cefuroxime (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-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, cystitis and urethritis
- skin and soft tissue infections for example, furunculosis, pyoderma and impetigo
- gonorrhoea, acute uncomplicated gonococcal urethritis, and cervicitis.
- treatment of early Lyme disease and subsequent prevention of late Lyme disease in adults and children over 12 years old.

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 to 10 days).

ZINNAT should be taken after food for optimum absorption.

• Adults

<table>
<thead>
<tr>
<th>Indication</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>125 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>
<tr>
<td>Lyme disease in adults and children over the age of 12 years</td>
<td>500 mg twice daily for 20 days</td>
</tr>
</tbody>
</table>

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

Acute exacerbations of chronic bronchitis
750 mg ZINACEF three times a day or twice a day (iv or im) for 48 to 72 hours, followed by ZINNAT (cefuroxime axetil) oral therapy 500 mg twice a day for 5 to 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
Most infections: 125 mg (1 x 125 mg tablet) twice daily, to a maximum of 250 mg daily.

Children aged two years or older with otitis media or, where appropriate, with more severe infections:
250 mg (1 x 250 mg tablet or 2 x 125 mg tablets) twice daily, to a maximum of 500 mg daily. ZINNAT tablets should not be crushed and are therefore unsuitable for treatment of patients, such as younger children, who cannot swallow tablets. In children ZINNAT oral suspension may be used. There is no experience of using ZINNAT in children under the age of 3 months.

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

The Jarisch-Herxheimer reaction has been seen following ZINNAT treatment of Lyme disease. It results directly from the bactericidal activity of ZINNAT on the causative organism of Lyme disease, the spirochaete Borrelia burgdorferi. Patients should be reassured that this is a common and usually self-limiting consequence of antibiotic treatment of Lyme disease.

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.

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 post-prandial 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 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 <1/1000) 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 in 10
- common: ≥1 in 100 and <1 in 10
- uncommon: ≥1 in 1,000 and <1 in 100
- rare: ≥1 in 10,000 and <1 in 1,000
- 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

**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 (exanthematous 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.

**PHARMACOLOGICAL 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 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.

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)
The absorption of cefuroxime from the suspension is more prolonged compared with tablets, leading to later, lower peak serum levels and slightly reduced systemic bioavailability (4-17% less). 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.

Pre-clinical Safety Data
No additional data of relevance.

PHARMACEUTICAL PARTICULARS
List of Excipients
Microcrystalline cellulose.
Croscarmellose sodium.
Hypermellose
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
The expiry date is indicated on the packaging.

Special Precautions for Storage
ZINNAT tablets should be stored at temperatures not exceeding 30oC.

Nature and Contents of Container
As registered locally.

Instructions for Use/Handling
None.

Not all presentations are available in every country.
Cefuroxime

QUALITATIVE AND QUANTITATIVE COMPOSITION

ZINNAT Suspension contains granules of cefuroxime for oral suspension. Reconstitution of multidose bottles as directed yields a suspension containing 125 mg or 250 mg of cefuroxime (as cefuroxime axetil) in each 5 ml.

ZINNAT Sachets contain 125 mg or 250 mg granules of cefuroxime (as cefuroxime axetil) for single dose administration when reconstituted.

PHARMACEUTICAL FORM

Dry, white to off-white, tutti-frutti flavoured granules for oral suspension.

CLINICAL PARTICULARS

Indications

ZINNAT 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 susceptible 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, cystitis and urethritis
- skin and soft tissue infections for example, furunculosis, pyoderma and impetigo
- gonorrhoea, acute uncomplicated gonococcal urethritis, and cervicitis
- treatment of early Lyme disease and subsequent prevention of late Lyme disease in adults and children over 12 years old.

Dosage and Administration

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

For optimal absorption ZINNAT should be taken with food.

• Adults

Most infections 250 mg twice daily
Urinary tract infections 125 mg twice daily
Mild to moderate lower respiratory tract infections e.g. 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 1 g
Lyme disease in adults and children over the age of 12 years. 500 mg twice daily for 20 days

• Children

When prescription of a fixed dose is preferred, the recommended dose for most infections is 125 mg twice daily. In children aged two years or older with otitis media or where appropriate, with more severe infections, the dose is 250 mg twice daily, to a maximum of 500 mg daily.

There are no clinical trial data available on the use of ZINNAT in children under the age of 3 months.

In infants and children, it may be preferable to adjust dosage according to weight or age.

The dose in infants and children 3 months to 12 years is 10 mg/kg twice daily for most infections, to a maximum of 250 mg daily. In otitis media or more severe infections the recommended dose is 15 mg/kg twice daily to a maximum of 500 mg daily.

The following two tables, divided by age group and weight, serve as a guideline for simplified administration from measuring spoons (5 ml) for the 125 mg/5 ml or the 250 mg/5 ml multi-dose suspension, and 125 mg or 250 mg single dose sachets.
10 mg/kg dosage for most infections

<table>
<thead>
<tr>
<th>Age</th>
<th>Approximate weight range (kg)</th>
<th>Dose mg twice daily</th>
<th>No. of measuring spoons (5 ml) or sachets per dose</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>125 mg</td>
</tr>
<tr>
<td>3 months - 6 months</td>
<td>4 - 6</td>
<td>40 - 60</td>
<td>½</td>
</tr>
<tr>
<td>6 months - 2 years</td>
<td>6 - 12</td>
<td>60 - 120</td>
<td>½ - 1</td>
</tr>
<tr>
<td>2 years - 12 years</td>
<td>12 - &gt;20</td>
<td>125</td>
<td>1</td>
</tr>
</tbody>
</table>

15 mg/kg dosage for otitis media and more serious infections

<table>
<thead>
<tr>
<th>Age</th>
<th>Approximate weight range (kg)</th>
<th>Dose mg twice daily</th>
<th>No. of measuring spoons (5 ml) or sachets per dose</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>125 mg</td>
</tr>
<tr>
<td>3 months - 6 months</td>
<td>4 - 6</td>
<td>60 - 90</td>
<td>½</td>
</tr>
<tr>
<td>6 months - 2 years</td>
<td>6 - 12</td>
<td>90 - 180</td>
<td>1 - ½</td>
</tr>
<tr>
<td>2 years - 12 years</td>
<td>12 - &gt;20</td>
<td>180 - 250</td>
<td>1 ½ - 2</td>
</tr>
</tbody>
</table>

To enhance compliance and improve the dosing accuracy in very young children, a dosing syringe can be supplied with a multidose bottle containing 50 ml of suspension.

However, dosing in spoonfuls should be considered a more favourable option if the child is able to take the medication from the spoon.

If required, the dosing syringe may also be used in older children (please refer to the dosing tables below).

The recommended doses for the paediatric dosing syringe are expressed in ml or mg and according to bodyweight in the following tables.

10 mg/kg/dose (Paediatric dosing syringe)

<table>
<thead>
<tr>
<th>Child’s weight (kg)</th>
<th>Dose twice daily (mg)</th>
<th>125 mg/5 ml dose twice daily (ml)</th>
<th>250 mg/5 ml dose twice daily (ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>40</td>
<td>1.6</td>
<td>0.8</td>
</tr>
<tr>
<td>6</td>
<td>60</td>
<td>2.4</td>
<td>1.2</td>
</tr>
<tr>
<td>8</td>
<td>80</td>
<td>3.2</td>
<td>1.6</td>
</tr>
<tr>
<td>10</td>
<td>100</td>
<td>4.0</td>
<td>2.0</td>
</tr>
<tr>
<td>12</td>
<td>120</td>
<td>4.8</td>
<td>2.4</td>
</tr>
<tr>
<td>14</td>
<td>140</td>
<td>5.6</td>
<td>2.8</td>
</tr>
</tbody>
</table>

15 mg/kg/dose (Paediatric dosing syringe)

<table>
<thead>
<tr>
<th>Child’s weight (kg)</th>
<th>Dose twice daily (mg)</th>
<th>125 mg/5 ml dose twice daily (ml)</th>
<th>250 mg/5 ml dose twice daily (ml)</th>
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</thead>
<tbody>
<tr>
<td>4</td>
<td>60</td>
<td>2.4</td>
<td>1.2</td>
</tr>
<tr>
<td>6</td>
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<td>3.6</td>
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<td>120</td>
<td>4.8</td>
<td>2.4</td>
</tr>
<tr>
<td>10</td>
<td>150</td>
<td>6.0</td>
<td>3.0</td>
</tr>
<tr>
<td>12</td>
<td>180</td>
<td>7.2</td>
<td>3.6</td>
</tr>
<tr>
<td>14</td>
<td>210</td>
<td>8.4</td>
<td>4.2</td>
</tr>
</tbody>
</table>

ZINNAT is also available as the sodium salt (ZINACEF) for parenteral administration. This permits parenteral therapy with ZINNAT to be followed by oral therapy in situations where a change from parenteral to oral treatment is clinically indicated.

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

The sucrose content of ZINNAT suspension and granules (see List of Excipients) should be taken into account when treating diabetic patients, and appropriate advice provided.

The Jarisch-Herxheimer reaction has been seen following ZINNAT treatment of Lyme disease. It results directly from the bactericidal activity of ZINNAT on the causative organism of Lyme disease, the spirochaete Borrelia burgdorferi. Patients should be reassured...
that this is a common and usually self-limiting conse-
quence of antibiotic treatment of Lyme disease.

**ZINNAT** suspension contains aspartame, which is a
source of phenylalanine and so should be used with
cautions in patients with phenylketonuria.

**Interactions**

Drugs which reduce gastric acidity may result in a
lower bioavailability of cefuroxime compared with
that of the fasting state and tend to cancel the effect
of enhanced absorption after food.

In common with other antibiotics, **ZINNAT** may
affect the gut flora, leading to lower oestrogen reab-
sorption and reduced efficacy of combined oral con-
traceptives.

As a false negative result may occur in the ferricya-
nide test, it is recommended that either the glucose
oxidase or hexokinase methods are used to deter-
mine blood/plasma glucose levels in patients receiv-
ing **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 cau-
tion during the early months of pregnancy. **ZINNAT**
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 cefuroxime axetil are gen-
erally 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 asso-
ciated with cefuroxime axetil may vary according to
the indication.

Data from large clinical studies were used to deter-
mine the frequency of very common to rare undesir-
able effects. The frequencies assigned to all other
undesirable effects (i.e. those occurring at <1/1000)
were mainly determined using post-marketing data
and refer to a reporting rate rather than true fre-
quency. Placebo-controlled trial data were not avail-
able. 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 in 10
- common: ≥1 in 100 and <1 in 10
- uncommon: ≥1 in 1,000 and <1 in 100
- rare: ≥1 in 10,000 and <1 in 1,000
- very rare: <1/10,000.

**Infections and infestations**

- Common: Overgrowth of Candida

**Blood and lymphatic system disorders**

- Common: Eosinophilia

- Uncommon: Positive Coombs’ test, thrombocytope-
nia, leukopenia (sometimes profound)

- Very rare: 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
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 (exantheme 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.

PHARMACOLOGICAL PROPERTIES
Pharmacodynamics
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 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.
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 (including penicillinase producing strains but excluding methicillin resistant strains)
Staphylococcus epidermidis (including penicillinase producing strains but excluding methicillin resistant strains)
Streptococcus pyogenes (and other β-haemolytic streptococci)
Streptococcus pneumoniae
Streptococcus Group B (Streptococcus agalactiae).

Anaerobes:
Gram-positive cocci and Gram-negative cocci (including Peptococcus and Peptostreptococcus species)
Gram-positive bacilli (including Clostridium species)
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.
Pharmacokinetics
After oral administration ZINNAT is absorbed from the gastrointestinal tract and rapidly hydrolysed in the intestinal mucosa and blood to release cefuroxime into the circulation.
Following administration of ZINNAT tablets peak serum levels (2.9 mg/l for a 125 mg dose, 4.4 mg/l for a 250 mg dose, 7.7 mg/l for a 500 mg dose and 13.6 mg/l for a 1 g dose) occur approximately 2.4 hours after dosing when taken with food.
Absorption of cefuroxime is enhanced in the presence of food. The rate of absorption of cefuroxime from the suspension compared with the tablets is reduced, leading to later, lower peak serum levels and reduced systemic bioavailability (4-17% less).
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.

Pre-clinical Safety Data
Animal toxicity studies indicated that cefuroxime is of low toxicity with no significant findings.

PHARMACEUTICAL PARTICULARS
List of Excipients
Aspartame.
Xanthan gum.
Acesulfame potassium.
Povidone K30.
Stearic acid.
Sucrose.
Tutti frutti flavour.

Sucrose Quantities:

<table>
<thead>
<tr>
<th>Sucrose quantity (g per dose)</th>
<th>125 mg/5 ml Suspension</th>
<th>250 mg/5 ml Suspension</th>
<th>125 mg Sachet</th>
<th>250 mg Sachet</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.062 g</td>
<td>2.289 g</td>
<td>3.062 g</td>
<td>6.123 g</td>
<td></td>
</tr>
</tbody>
</table>

Incompatibilities
None.

Shelf Life
The expiry date of the granules is indicated on the packaging.
The reconstituted suspension when refrigerated between 2 and 8oC can be kept for up to 10 days.

Special Precautions for Storage
The reconstituted suspension must be refrigerated immediately at between 2 and 8oC.

Nature and Contents of Container
Multidose bottles:
ZINNAT Suspension is supplied in PhEur Type III amber glass bottles with an induction heat seal membrane containing either 125 mg/5 ml or 250 mg/5 ml product. Dosing syringes are available with multidose bottles of both strengths.

Sachets:
ZINNAT Suspension in sachets for oral use is supplied in paper/polyethylene/foil/ethylenemethacrylic acid ionomer laminated sachet. When reconstituted as directed, it provides the equivalent of 125 mg or 250 mg of ZINNAT (as cefuroxime axetil) per sachet.

Instructions for Use/Handling
• Constitution/Administration Instructions
Always shake the bottle vigorously before taking the medication.
The reconstituted suspension when refrigerated between 2 and 8oC can be kept for up to 10 days.
If desired ZINNAT suspension can be further diluted suspension from multidose bottles in cold fruit juices, or milk drinks and should be taken immediately.
The reconstituted suspension or granules should not be mixed with hot liquids.

• Directions for reconstituting suspension in multidose bottles
1. Shake the bottle to loosen the granules. Remove the cap and the heat-seal membrane.
If the latter is damage or not present, the product should be returned to the pharmacist.
2. Add the total amount of water to the bottle as stated on its label. Replace the cap.
3. Invert the bottle and rock vigorously (for at least 15 seconds) as shown below.
4. Turn the bottle into an upright position and shake vigorously.
5. Refrigerate immediately at between 2 and 8°C.
6. If using a dosing syringe, allow the reconstituted suspension to stand for at least one hour before taking the first dose.

• Directions for using the dosing syringe
  1. Remove the bottle cap and insert the syringe-collar assembly into the neck of the bottle. Press it down completely until the collar fits in the neck firmly.
  2. Pull the plunger up the barrel until the barrels rim is aligned with the mark on the plunger corresponding to the required dose.
  3. While holding onto the syringe and the plunger to ensure that the plunger does not move, remove the syringe from the bottle, leaving the plastic collar in the bottle neck.
  4. With the patient seated in an upright position, place the tip of the syringe just inside the patients mouth, pointing towards the inside of the cheek.
  5. Press the plunger of the syringe in slowly to expel the medicine without causing choking. Do NOT squirt the medicine out in a jet.
  6. After giving the dose replace the bottle cap without removing the plastic collar.

Dismantle the syringe and wash it thoroughly in fresh drinking water. Allow the plunger and the barrel to dry naturally.

• Directions for reconstituting suspension from sachets
  1. Empty granules from sachet into a glass.
  2. Add a small volume of water.
  3. Stir well and drink immediately.

Not all presentations are available in every country.

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