PRODUCT INFORMATION
ZINNAT® SUSPENSION

NAME OF THE MEDICINE

Cefuroxime axetil

Cefuroxime axetil is the 1-(acetyloxy)ethyl ester of cefuroxime. Its chemical name is (RS)-1-hydroxyethyl(6R,7R)-7-[2-(2-furyl)glyoxylamido]-3-(hydroxymethyl)-8-oxo-5-thia-1-azabicyclo[4.2.0]-oct-2-ene-2-carboxylate, 72)–(Z)–(O-methyloxime), 1-acetate 3-carbamate. Its molecular formula is C20H22N4O10S, and it has a molecular weight of 510.48.

Cefuroxime axetil is in the amorphous form, and it has the following structural formula:

\[
\begin{align*}
\text{CH}_3 & \quad \text{OCONH} \\
\text{NOCH}_3 & \quad \text{H} \\
\text{CONH} & \quad \text{C} \\
\text{CH}_2\text{OCONH}_2 & \quad \text{CH}_3 \\
\text{CO}_2\text{CHOCOCH}_3 & \quad \text{CH}_3
\end{align*}
\]

Chiral centre at C*

CAS Registry Number : 64544-07-6

PHARMACOLOGY

Mode of action

Cefuroxime axetil is a semisynthetic broad-spectrum cephalosporin. It is a prodrug which owes its in vivo bactericidal activity to the release of the active compound cefuroxime.

Cefuroxime has bactericidal activity against a wide range of common pathogens, including beta-lactamase producing strains. The bactericidal action of cefuroxime results from inhibition of cell wall synthesis by binding to essential target proteins. Cefuroxime has good stability to bacterial beta-lactamases.

Clinical Trials

Otitis media

Three pivotal, multi-centre, investigator-blind, randomised clinical studies (CAE 331, CAE 331/Howie, CAE 332) evaluated cefuroxime axetil suspension, 30mg/kg/day in two divided doses for 10 days, in the treatment of otitis media with effusion in 261 paediatric patients aged 3 months to 12 years. The comparator agent was amoxycillin/clavulanate suspension 40mg/kg/day in three divided doses for 10 days (n=139). Comparable rates of clinical cure/improvement (82.4% and 79.7% for cefuroxime axetil and amoxycillin/clavulanate respectively) and bacteriological cure (93% and 96% for cefuroxime axetil and amoxycillin/clavulanate respectively) were obtained with the two treatment regimens in the evaluable population.

An open, randomised multi-centre study (CAET95) comparing cefuroxime axetil suspension (250mg [125mg if < 2 years old] twice daily) with amoxycillin syrup (250mg [125mg if <2 years old] three times daily) for 10 days in 660 children showed comparable
rates of clinical response to both antibiotics (94-95%) in clinically evaluable patients. Bacteriological clearance rates were similar (96.9% for cefuroxime axetil vs 95% for amoxycillin, p>0.05) in the limited number of patients (approximately 10%) who had positive ear swabs or who underwent tympanocentesis.

An open, randomised, multicentre study (CAEB 4006) to compare the efficacy and safety of a 5-day course of cefuroxime axetil suspension with an 8- or 10-day course of amoxicillin/clavulanate suspension was conducted in 716 children aged between 6 and 36 months suffering from otitis media with effusion. The patients were randomised to receive cefuroxime axetil 30mg/kg/day in two divided doses for 5 days (n=252), amoxicillin/clavulanate 40mg/kg/day in three divided doses for 10 days (n=255), or amoxicillin/clavulanate 80mg/kg/day in three divided doses for 8 days (n=209). In the clinical evaluable population, the proportion of patients with clinical cure at post treatment was 86%, 88% and 88% for each of the groups respectively. Statistical equivalence was demonstrated between the three treatments (95% confidence intervals for cefuroxime axetil treatment vs 10-day and 8-day amoxicillin treatments were –9.0% to 4.8% and –9.5% to 5.1% respectively).

Tonsillopharyngitis
Two, randomised, multi-centre studies (CAE 333, CAE 334) were conducted, in which 509 children aged 2 to 12 years with tonsillopharyngitis and a positive throat culture for Group A streptococci were treated for 10 days with either cefuroxime axetil suspension 20mg/kg/day in two divided doses or penicillin V syrup 50mg/kg/day in three divided doses. Clinical efficacy was demonstrated in a higher proportion of cefuroxime axetil-treated patients in both intent-to-treat and evaluable populations (80% vs 71% in ITT population, p=0.008; 91% vs 83% in evaluable patients, p=0.013). A bacteriological cure (eradication or presumed eradication of Group A streptococci) or cure with reinfection was achieved in 84% of cefuroxime axetil treated patients compared to 77% treated with penicillin V. Similar overall adverse event rates were reported for both treatments (p = 0.05).

One open-label, multi-centre study (CAET94) was conducted in 633 children, in which seven days of treatment with cefuroxime axetil suspension (62.5mg twice daily in children <2 years and 125mg twice daily in children >2 years) was compared to seven days of treatment with amoxycillin syrup (125mg three times daily). Clinical cure or improvement occurred in 95% of evaluable patients treated with cefuroxime axetil compared to 97% treated with amoxycillin. Approximately 30% of patients were bacteriologically evaluable. In this subgroup, similar levels of bacteriological clearance were achieved with the two agents (95% vs 87%, not statistically significant).

An open, randomised, multi-centre study (CAEB 4007) of 406 children with confirmed Group A streptococcal tonsillopharyngitis demonstrated that 5 days of treatment with cefuroxime axetil suspension 20mg/kg twice daily was equivalent to a 10-day course of treatment in eradication of the pathogen (88% vs 92%, 95% confidence interval –10% to 3%). At 21-28 day follow-up, bacterial eradication was maintained in 85% of patients in the 5-day group and 87% of patients in the 10-day group. Equivalence was also demonstrated for clinical cure rates at post-treatment assessment (96% vs 98%, 95% confidence interval –7% to 2%).
Microbiology
Cefuroxime has been shown to be usually active against the following organisms in vitro and in clinical studies:

**Aerobic Gram-negative Microorganisms:**
- *Escherichia coli*
- *Haemophilus influenzae* (including beta-lactamase-producing strains)
- *Haemophilus parainfluenzae*
- *Klebsiella pneumoniae*
- *Moraxella catarrhalis* (including beta-lactamase-producing strains)
- *Neisseria gonorrhoeae* (including beta-lactamase producing strains)

**Aerobic Gram-positive Microorganisms:**
- *Staphylococcus aureus* (including penicillinase producing strains but excluding methicillin resistant strains)
- *Streptococcus pyogenes* (and other beta-haemolytic streptococci)
- *Streptococcus pneumoniae*

Cefuroxime exhibits in vitro minimum inhibitory concentrations (MICs) of 4.0 μg/mL or less (systemic susceptible breakpoint) against most (≥90%) strains of the following microorganisms; however, the clinical significance of these findings is unknown:

**Aerobic Gram-positive Microorganisms:**
- *Staphylococcus epidermidis*
- *Staphylococcus saprophyticus*
- *Streptococcus agalactiae*

**Aerobic Gram-negative Microorganisms**
- *Proteus inconstans*
- *Proteus mirabilis*
- *Providencia rettgeri*

**Anaerobic Microorganisms:**
- *Peptococcus niger*

The following organisms are not susceptible to cefuroxime:
- *Clostridium difficile*
- Pseudomonas spp
- Campylobacter spp
- *Acinetobacter calcoaceticus*
- *Morganella morganii*
- *Listeria monocytogenes*
- Methicillin resistant strains of *Staphylococcus aureus* and *Staphylococcus epidermidis*
- *Legionella* spp
- *Proteus vulgaris*
- Serratia spp
- *Bacteroides fragilis*
- Most strains of *Enterococcus faecalis*
- *Citrobacter* spp
- *Enterobacter* spp
Table 1 - Acquired resistance to cefuroxime (axetil) in organisms frequently encountered in otitis media and upper respiratory tract infections – Australian isolates

<table>
<thead>
<tr>
<th>Organism</th>
<th>Number of strains</th>
<th>Percentage of Strains</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Intermediate</td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All isolates</td>
<td>142</td>
<td>4</td>
</tr>
<tr>
<td>Penicillin susceptible</td>
<td>102</td>
<td>1</td>
</tr>
<tr>
<td>Penicillin intermediate</td>
<td>25</td>
<td>4</td>
</tr>
<tr>
<td>Penicillin resistant</td>
<td>15</td>
<td>0</td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All isolates</td>
<td>218</td>
<td>0.5</td>
</tr>
<tr>
<td>Beta-lactamase positive</td>
<td>48</td>
<td>0</td>
</tr>
</tbody>
</table>

No Australian data is available for *Streptococcus pyogenes*. However, worldwide, no resistance to cefuroxime or other beta-lactam antibiotics has been reported. Cefuroxime is active against macrolide-resistant strains.

For cefuroxime axetil in common with other cephalosporins, the time that drug concentrations exceed MIC correlates most closely with clinical efficacy. For a given cefuroxime MIC, drug concentrations maintained for 30%-40% of the dosing interval are likely to be effective in patients with community-acquired infections.

In patients with tonsillopharyngitis caused by *S. pyogenes* with MIC90 0.015mcg/ml, cefuroxime concentrations t>MIC is likely to be >10 hours.

In patients with otitis media treated with 15mg/kg/dose, organisms within the MIC range <0.06- 2 micrograms/ml would be expected to be amenable to treatment - see table below derived from fasting subjects. Administration immediately after food would be expected to increase absorption.

Table 2: T>MIC for a dose of a 15mg/kg in fasted patients with otitis media

<table>
<thead>
<tr>
<th>MIC μg/ml</th>
<th>T&gt;MIC (Hours)</th>
<th>%Dosing interval T&gt;MIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.06</td>
<td>12</td>
<td>100%</td>
</tr>
<tr>
<td>0.25</td>
<td>8.5</td>
<td>71%</td>
</tr>
<tr>
<td>0.5</td>
<td>7.0</td>
<td>58%</td>
</tr>
<tr>
<td>1.0</td>
<td>4.7</td>
<td>39%</td>
</tr>
<tr>
<td>2.0</td>
<td>3.0</td>
<td>25%</td>
</tr>
</tbody>
</table>

In a study of pharmacokinetics in paediatric patients with otitis media, dosed after food at 15mg/kg, serum concentrations exceeded a MIC of 2μg/ml for at least 5 hours (42%) of the dosing interval. (Thoroddsen E. et al. Ped Inf Dis 1997;16:959-962).

Cefuroxime axetil susceptibility relevant to the indications are as follows:

*S.pyogenes*  MIC90 0.015  100% European strains  
*S.pneumoniae*  MIC90 ≤1μg/ml*  99% of Australian isolates
**Susceptibility tests**

Dilution or diffusion techniques – either quantitative (MIC) or breakpoint, should be used following a regularly updated, recognised and standardised method (eg. NCCLS). Standardised susceptibility test procedures require the use of the laboratory control microorganisms to control the technical aspects of the laboratory procedures.”

A report of “Susceptible” indicates that the pathogen is likely to be inhibited if the antimicrobial compound in the blood reaches the concentrations usually achievable. A report of “Intermediate” indicates that the result should be considered equivocal, and if the microorganism is not fully susceptible to alternative, clinically feasible drugs, the test should be repeated.

This category implies possible clinical applicability in body sites where the drug is physiologically concentrated or in situations where high dosage of drug can be used. This category also provides a buffer zone, which prevents small uncontrolled technical factors from causing major discrepancies in interpretation. A report of “Resistant” indicates that the pathogen is not likely to be inhibited if the antimicrobial compound in the blood reaches the concentrations usually achievable; other therapy should be selected.

**Pharmacokinetics**

After oral administration cefuroxime axetil is absorbed from the gastrointestinal tract and rapidly hydrolysed in the intestinal mucosa and blood to release cefuroxime into the circulation. 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 than the 60% bioavailability seen with tablets). Absorption of cefuroxime axetil suspension is enhanced in the presence of food. Absorption is not decreased by drugs which affect gastrointestinal motility eg loperamide, diphenoxylate or castor oil. However, absorption is decreased by concurrent administration of drugs which reduce gastric acidity.

The mean peak serum level of cefuroxime following dosing with a 250mg tablet in normal healthy adults, after food, was 4.1mg/L and occurred two to three hours after dosing. Serum levels were significantly higher in the elderly, apparently due to slower excretion.

Unhydrolysed drug has not been detected in the serum but 1-2% of the administered dose is excreted in the urine in a form which indicates that small amounts of the intact ester are absorbed into circulation. The serum half-life of cefuroxime 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 to any significant extent.

Excretion occurs mainly through the kidney both by glomerular filtration and tubular secretion. Approximately 49% of an administered dose, after food, is recovered in the urine in 24 hours; urinary recovery is significantly reduced if the drug is taken on an empty stomach. After a 250mg dose urinary concentrations at 0-6 and 6-12 hours were 227µg/mL (range 92-515) and 35.3µg/mL (range 7.6-102) respectively.

**Table 3**: Pharmacokinetic parameters determined after single doses of 10 and 15 mg/kg cefuroxime axetil suspension in paediatric patients aged 3 months to 12 years:
Parameter | Dose (mg/kg) | 10 | 15 |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=8</td>
<td>n=12</td>
<td></td>
</tr>
<tr>
<td>C&lt;sub&gt;max&lt;/sub&gt; (μg/ml)</td>
<td>3.3</td>
<td>5.1</td>
<td></td>
</tr>
<tr>
<td>T&lt;sub&gt;max&lt;/sub&gt; (h)</td>
<td>3.6</td>
<td>2.7</td>
<td></td>
</tr>
<tr>
<td>AUC&lt;sub&gt;∞&lt;/sub&gt; (μg.h/ml)</td>
<td>12.4</td>
<td>22.5</td>
<td></td>
</tr>
<tr>
<td>T&lt;sub&gt;1/2&lt;/sub&gt; (h)</td>
<td>1.4</td>
<td>1.9</td>
<td></td>
</tr>
</tbody>
</table>

The pharmacokinetic parameters were not significantly affected by patient age or weight. C<sub>max</sub> and AUC<sub>∞</sub> increased proportionately with dose in a linear relationship over the dose range 10-20mg/kg.

**INDICATIONS**

ZINNAT suspension is indicated for the treatment of the following mild to moderately severe infections caused by sensitive bacteria in paediatric patients 3 months to 12 years; tonsillitis and pharyngitis, acute bacterial otitis media.

Penicillin is the usual drug of choice in the treatment and prevention of streptococcal infections, including the prophylaxis of rheumatic fever. Cefuroxime axetil appears to be as effective as phenoxyacetylpenicillin in the eradication of streptococci from the nasopharynx. However, substantial data establishing the efficacy of cefuroxime axetil in the subsequent prevention of rheumatic fever is not available at present.

**CONTRAINDICATIONS**

Patients with known hypersensitivity to cephalosporin antibiotics or who have experienced a major allergy to penicillin (anaphylaxis, angioneurotic oedema, urticaria).

**PRECAUTIONS**

Serious and occasionally fatal hypersensitivity (anaphylactic/anaphylactoid) reactions have been reported in patients on penicillin/cephalosporin therapy. Although anaphylaxis is more frequent following parenteral therapy, it has occurred in patients on oral penicillins/cephalosporins. These reactions are more likely to occur in individuals with a history of penicillin hypersensitivity and/or a history of sensitivity to multiple allergens. There have been reports of individuals with a history of penicillin/cephalosporin hypersensitivity who have experienced severe reactions when treated with a penicillin/cephalosporins. Past history of a severe allergic reaction to penicillin/cephalosporin is a contraindication to the use of cefuroxime axetil. Before initiating therapy with any penicillin/cephalosporin careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, or other allergens. If an allergic reaction occurs, cefuroxime axetil should be discontinued and the appropriate therapy instituted. Serious anaphylactoid reactions require immediate emergency treatment with adrenaline. Oxygen, intravenous steroids, and airway management, including intubation, should also be administered as indicated.

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 (eg Enterococci and Clostridium), which may require interruption of treatment.

Antibiotic associated pseudomembranous colitis has been reported with many antibiotics including cefuroxime axetil. A toxin produced by *Clostridium difficile* appears to be the primary cause. The severity of the colitis may range from mild to life threatening. It is important to consider this diagnosis in patients who develop diarrhoea or colitis in
association with antibiotic use (this may occur up to several weeks after cessation of antibiotic therapy). Mild cases usually respond to drug discontinuation alone although cholestyramine may help by binding the toxin in the colonic lumen. However, in moderate to severe cases appropriate therapy with a suitable oral antibacterial agent effective against *Clostridium difficile* should be considered. Fluids, electrolytes and protein replacement should be provided when indicated.

Drugs which delay peristalsis eg opiates and diphenoxylate with atropine (LOMOTIL) may prolong and/or worsen the condition and should not be used.

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

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

**Patients with Severe Renal Impairment:** There is no information on use of ZINNAT suspension in patients with renal impairment however the dosage of cefuroxime tablets in adults should not exceed 500mg per day and should be repeated after dialysis.

**Use in the Elderly:** The serum half life of cefuroxime is increased and plasma levels raised in elderly patients with declining renal function. No dosage reduction is necessary in such patients at recommended dosages.

**Use in Pregnancy:** Pregnancy Category: B1
There is no experimental evidence of embryopathic or teratogenic effects attributable to cefuroxime axetil. However, there is no clinical data on the use of cefuroxime axetil during pregnancy. Therefore it should be administered during pregnancy only if such use is considered essential.

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

**Ability to perform tasks that require judgement, motor or cognitive skills:** As this medicine may cause dizziness, patients should be warned to be cautious when driving or operating machinery.

**Interactions with Laboratory Tests**
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.

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

In common with other antibiotics, cefuroxime axetil may affect the gut flora, leading to lower oestrogen reabsorption and reduced efficacy of combined oral contraceptives.

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.

**ADVERSE EFFECTS**

Adverse reactions to cefuroxime axetil have been generally mild and transient in nature.
Clinical Trial Data

Table 4: The most common drug related adverse events reported in 9 clinical studies comparing cefuroxime axetil suspension to either amoxycillin, amoxycillin/clavulanate, penicillin V or cefadroxil containing products.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Cefuroxime Axetil</th>
<th>Amoxycillin</th>
<th>Amoxycillin / Clavulanate</th>
<th>Penicillin V</th>
<th>Cefadroxil</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose Range</td>
<td>20 – 30 mg/kg/day or 250 – 500mg/day</td>
<td>40 mg/kg/day or 250 – 500mg/day</td>
<td>*40 mg/kg/day</td>
<td>50 mg/kg/day</td>
<td>30 mg/kg/day</td>
</tr>
<tr>
<td>N</td>
<td>1525</td>
<td>643</td>
<td>144</td>
<td>212</td>
<td>88</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Body System &amp; Adverse Event</th>
<th>(%)</th>
<th>(%)</th>
<th>(%)</th>
<th>(%)</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhoea/loose stools</td>
<td>5.9</td>
<td>2.0</td>
<td>29.2</td>
<td>1.4</td>
<td>1.1</td>
</tr>
<tr>
<td>Nappy rash</td>
<td>0.8</td>
<td>0.5</td>
<td>6.9</td>
<td>0.0</td>
<td>3.4</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>2.2</td>
<td>1.1</td>
<td>2.1</td>
<td>0.5</td>
<td>1.1</td>
</tr>
<tr>
<td>Hyperactivity</td>
<td>0.1</td>
<td>0.5</td>
<td>0.0</td>
<td>0.5</td>
<td>1.1</td>
</tr>
</tbody>
</table>

* = Dose based on amoxycillin content.  NR = Not Reported

Post Marketing Data

The following adverse reactions to cefuroxime axetil are considered to be drug related and have been reported in clinical trials or post-marketing data. However, the possibility of the occurrence of other adverse reactions, seen with the cephalosporin class of antibiotics, should be borne in mind.

Gastrointestinal
A small proportion of patients receiving cefuroxime axetil have experienced gastrointestinal disturbances including diarrhoea, nausea, vomiting and abdominal pain. As with other broad-spectrum antibiotics there have been reports of pseudomembranous colitis.

Hepatic
Transient increases of hepatic enzyme levels [ALT (SGPT), AST (SGOT) and LDH]. As with other cephalosporins jaundice has been reported very rarely. Hepatitis has been reported.

CNS
Headache, dizziness.

Haematological
Eosinophilia, positive Coomb's test and in very rarely haemolytic anaemia. There have been rare reports of thrombocytopenia and leucopenia (sometimes profound).

Hypersensitivity
Patients with a history of delayed hypersensitivity to penicillin (but not a cephalosporin) experienced delayed hypersensitivity reaction to cefuroxime axetil in 2.9% cases.

As with other cephalosporins, rare cases of severe hypersensitivity reactions, including Stevens-Johnson syndrome, erythema multiforme, toxic epidermal necrolysis (exanthematic necrolysis) and hypersensitivity reactions including skin rashes, urticaria, pruritus, drug fever, serum sickness and very rarely, anaphylaxis have been reported with cefuroxime axetil.

Infections and infestations
**Candida** overgrowth has been reported commonly.

**DOSAGE AND ADMINISTRATION**

ZINNAT Tablets and ZINNAT Oral Suspension are not bioequivalent and are therefore not substitutable on a mg per mg basis (see Pharmacokinetics).

The usual course of therapy with ZINNAT suspension is 7 days (with a range of 5 to 10 days).

Cefuroxime axetil should be taken with a light meal for optimum absorption.

The recommended dose for most infections is 125 mg twice daily. In children aged two years or older with otitis media or where appropriate in children, with more severe infections, the dose is 250 mg twice daily.

There is no clinical experience with the use of ZINNAT in infants under the age of 3 months.

In infants and children, it may be preferable to adjust dosage according to weight or age. The dose of Zinnat Oral Suspension recommended for treatment of tonsillitis and pharyngitis is 10mg/kg twice daily, to a maximum of 250mg daily. The dose of Zinnat Oral Suspension recommended for the treatment of acute bacterial otitis media is 15mg/kg twice daily, to a maximum of 500mg daily.

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

**Table 5: 10 mg/kg dosage twice daily for tonsillitis and pharyngitis**

<table>
<thead>
<tr>
<th>Age</th>
<th>Approximate weight range (kg)</th>
<th>Dose (mg) twice daily</th>
<th>No. of measuring spoons (5mL) or sachets per dose</th>
</tr>
</thead>
<tbody>
<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>

**Table 6: 15 mg/kg dosage twice daily for otitis media**

<table>
<thead>
<tr>
<th>Age</th>
<th>Approximate weight range (kg)</th>
<th>Dose (mg) twice daily</th>
<th>No. of measuring spoons (5mL) or sachets per dose</th>
</tr>
</thead>
<tbody>
<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 – 1½</td>
</tr>
<tr>
<td>2 years – 12 years</td>
<td>12 – &gt;20</td>
<td>180 – 250</td>
<td>1½ - 2</td>
</tr>
</tbody>
</table>

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 damaged or not present, the product should not be used.
2. Add the total amount of water to the bottle as stated on its label and replace the cap.
3. Invert the bottle and vigorously rock the bottle from side to side so that water rises through the granules.
4. Once the sound of the granules against the bottle disappears, turn the bottle upright and shake vigorously.
5. Refrigerate the reconstituted suspension 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.
Always shake the bottle well before each use.

The reconstituted suspension when refrigerated immediately between 2° and 8°C can be kept for up to 10 days.

If desired ZINNAT suspension from multidose bottles can be further diluted in cold fruit juices or milk drinks and should be taken immediately.

**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.

The reconstituted suspension or granules from sachets should not be mixed with hot liquids.

**OVERDOSAGE**

Overdosage of cephalosporins can cause cerebral irritation leading to convulsions.

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

Contact the Poisons Information Centre (telephone 13 11 26) for advice on overdose management.

**PRESENTATION AND STORAGE CONDITIONS**

*Multidose bottles:* ZINNAT suspension is provided as a dry, white to off-white, tutti-frutti flavoured granule. When reconstituted as directed, it provides the equivalent of 125 mg or 250 mg of cefuroxime (as cefuroxime axetil) per 5 mL of suspension.

ZINNAT suspension is supplied in amber glass bottles containing either 50 mL, 70 mL, 100 mL or 200 mL of 125mg/5mL suspension or 50 mL, 70 mL or 100 mL of 250 mg/5 mL suspension.

*Sachets:* ZINNAT suspension is provided as dry, white to off-white, tutti-frutti flavoured granule in laminated sachets. When reconstituted as directed, it provides the equivalent of 125 mg or 250 mg of cefuroxime (as cefuroxime axetil) per dose.

Not all dose forms/container sizes are being distributed in Australia.

ZINNAT suspension also contains poly vinyl pyrrolidone (Povidone K30), stearic acid, sucrose, tutti-frutti flavour, acesulfame potassium, aspartame and xanthan gum.

**Table 7: Sucrose quantity (g per dose)**

<table>
<thead>
<tr>
<th>125mg/5mL suspension</th>
<th>250mg/5mL suspension</th>
<th>125mg sachet</th>
<th>250mg sachet</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.062g</td>
<td>2.289g</td>
<td>3.062g</td>
<td>6.123g</td>
</tr>
</tbody>
</table>

Store ZINNAT powder for suspension below 30°C.

The reconstituted suspension must be refrigerated immediately between 2° and 8°C.
NAME AND ADDRESS OF THE SPONSOR

GlaxoSmithKline Australia Pty Ltd
Level 4,
436 Johnston Street,
Abbotsford, Victoria, 3067
Australia

POISON SCHEDULE OF THE MEDICINE

Schedule 4 – Prescription Only Medicine

Date of TGA Approval: 27 April 2011
Date of last amendment: 2 November 2012

ZINNAT® is a registered trade mark of the GlaxoSmithKline group of companies

Version 3.0