Cefuroxime (as sodium)

Zinacef®
Powder for Injection
Antibacterial

PRODUCT DESCRIPTION
Cefuroxime (as sodium) (Zinacef®) 250mg Powder for Injection: Each white to faintly yellow powder to which appropriate amounts of water are added to prepare an off-white suspension for intramuscular (IM) use or a yellowish solution for intravenous (IV) administration contains 250mg of Cefuroxime as sodium.

Cefuroxime (as sodium) (Zinacef®) 750mg Powder for Injection: Each white to faintly yellow powder to which appropriate amounts of water are added to prepare an off-white suspension for intramuscular (IM) use or a yellowish solution for intravenous (IV) administration contains 750mg of Cefuroxime as sodium.

Cefuroxime (as sodium) (Zinacef®) 1.5g Powder for Injection: Each white to faintly yellow powder to which appropriate amounts of water are added to prepare an off-white suspension for intramuscular (IM) use or a yellowish solution for intravenous (IV) administration contains 1.5g of Cefuroxime as sodium.

Variations in the intensity of this color do not indicate any change in either the efficacy or safety of the product.

PHARMACOLOGIC PROPERTIES
Pharmacodynamics
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. 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.

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<td>Neisseria gonorrhoea* including penicillin and non-penicillinase producing strains</td>
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<td>Neisseria meningitidis</td>
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<td>Shigella spp.</td>
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<td>Bordetella pertussis</td>
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<td>Escherichia coli*</td>
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<td>Klebsiella spp. including K. pneumoniae*</td>
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<td>Proteus mirabilis</td>
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<td>Providencia spp.</td>
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<td>Salmonella spp.</td>
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<td>Clostridium spp. not including C. difficile</td>
</tr>
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<td>Gram-Negative Anaerobes:</td>
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**Bacteroides spp. not including B. fragilis**
**Fusobacterium spp.**

**Inherently resistant organisms**

**Gram-Positive Aerobes:**
- Enterococcus spp. including *E. faecalis* and *E. faecium*
- *Listeria monocytogenes*

**Gram-Negative Aerobes:**
- *Acinetobacter spp.*
- *Burkholderia cepacia*
- *Campylobacter spp.*
- *Citrobacter freundii*
- *Enterobacter aerogenes*
- *Enterobacter cloacae*
- *Morganella morganii*
- *Proteus penneri*
- *Proteus vulgaris*
- *Pseudomonas spp. including* *P. aeruginosa*
- *Serratia spp.*
- *Stenotrophomonas maltophilia*

**Gram-Positive Anaerobes:**
- *Clostridium difficile*

**Gram-Negative Anaerobes:**
- *Bacteroides fragilis*

**Others:**
- *Chlamydia species*
- *Mycoplasma species*
- *Legionella species*

**Pharmacokinetics**

Peak levels of cefuroxime are achieved within 30 to 45 minutes after i.m. administration. Protein binding has been variously stated as 33 - 50% depending on the methodology used. Concentrations of cefuroxime in excess of the minimum inhibitory levels for common pathogens can be achieved in bone, synovial fluid and aqueous humour. Cefuroxime passes the blood-brain barrier when the meninges are inflamed. Cefuroxime is not metabolised and is excreted by glomerular filtration and tubular secretion. The serum half-life after either i.m. or i.v. injection is approximately 70 minutes. In the first weeks of life the serum half-life of cefuroxime can be 3 to 5 times that in the adult. Concurrent administration of probenecid prolongs the excretion of the antibiotic and produces an elevated peak serum level. There is an almost complete recovery (85 to 90%) of unchanged cefuroxime in urine within 24 hours of administration. The major part is excreted in the first 6 hours. Serum levels of cefuroxime are reduced by dialysis.

**Pre-clinical Safety Data**

No additional data of relevance.

**INDICATIONS**

Cefuroxime (as sodium) (*Zinacef*®) is a bactericidal cephalosporin antibiotic 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 before the infecting organism has been identified or when caused by sensitive bacteria. Susceptibility to Cefuroxime (as sodium) (*Zinacef*®) will vary with geography and time and local susceptibility data should be consulted where available (see Pharmacological properties, Pharmacodynamics).

Indications include:
- respiratory tract infections for example, acute and chronic bronchitis, infected bronchiectasis, bacterial pneumonia, lung abscess and post-operative chest infections
- ear, nose and throat infections for example, sinusitis, tonsillitis, pharyngitis and otitis media
- urinary tract infections for example, acute and chronic pyelonephritis, cystitis and asymptomatic bacteriuria
- soft-tissue infections for example, cellulitis, erysipelas and wound infections
- bone and joint infections for example, osteomyelitis and septic arthritis
- obstetric and gynaecological infections, pelvic inflammatory diseases
- gonorrhoea particularly when penicillin is unsuitable
- other infections including septicaemia, meningitis and peritonitis
- prophylaxis against infection in abdominal, pelvic, orthopaedic, cardiac, pulmonary, oesophageal and vascular surgery where there is increased risk from infection.

Usually Cefuroxime (as sodium) (*Zinacef*®) will be effective alone, but when appropriate it may be used in combination with an aminoglycoside antibiotic, or in conjunction with metronidazole (orally or by suppository or injection), especially for prophylaxis in colonic or gynaecological surgery.

Where appropriate Cefuroxime (as sodium) (*Zinacef*®) is effective when used prior to oral therapy with Cefuroxime (as axetil) (*Zinnat*®) in the treatment of pneumonia and acute exacerbations of chronic bronchitis.
DOSE & ADMINISTRATION
Cefuroxime (as sodium) (Zinacef®) Injection is for intravenous (i.v.) and/or intramuscular (i.m.) administration. Cefuroxime (as sodium) (Zinacef®) is also available as the axetil ester Cefuroxime (as axetil) (Zinacef®) for oral administration. This permits the use of sequential therapy with the same antibiotic, when a change from parenteral to oral therapy is clinically indicated.

GENERAL DOSING RECOMMENDATIONS
- **Adults**
  Many infections respond to 750 mg three times daily by i.m. or i.v. injection. For more severe infections the dose should be increased to 1.5 g three times daily given i.v. The frequency of administration may be increased to 6-hourly if necessary, giving total daily doses of 3 to 6 g. Where clinically indicated, some infections respond to 750 mg or 1.5 g twice daily (i.v. or i.m.) followed by oral therapy with Cefuroxime (as axetil) (Zinacef®).

- **Infants and Children**
  - 30 to 100 mg/kg/day given as 3 or 4 divided doses. A dose of 60 mg/kg/day is appropriate for most infections.
  - **Neonates**
    - 30 to 100 mg/kg/day given as 2 or 3 divided doses (see Pharmacokinetics).

GONORRHOEA
- **Adults**
  1.5 g as a single dose (as 2 x 750 mg injections given i.m. with different sites e.g. each buttock).

MENINGITIS
Cefuroxime (as sodium) (Zinacef®) is suitable for sole therapy of bacterial meningitis due to sensitive strains.

- **Adults:**
  - 3 g given i.v. every 8 hours.
- **Infants and Children:**
  - 150 to 250 mg/kg/day given i.v. in 3 or 4 divided doses
- **Neonates:**
  - the dosage should be 100 mg/kg/day given i.v.

PROPHYLAXIS
The usual dose is 1.5 g given i.v. with induction of anaesthesia for abdominal, pelvic and orthopaedic operations. This may be supplemented with two 750 mg i.m. doses 8 and 16 hours later. In cardiac, pulmonary, oesophageal and vascular operations, the usual dose is 1.5 g given i.v. with induction of anaesthesia, continuing with 750 mg given i.m. three times daily for a further 24 to 48 hours.

In total joint replacement, 1.5 g Cefuroxime (as sodium) (Zinacef®) powder may be mixed dry with each pack of methyl methacrylate cement polymer before adding the liquid monomer.

SEQUENTIAL THERAPY
- **Adults**
  Duration of both parenteral and oral therapy is determined by the severity of the infection and the clinical status of the patient.

Pneumonia
1.5 g Cefuroxime (as sodium) (Zinacef®) three times daily or twice daily (given i.v. or i.m.) for 48 to 72 hours, followed by 500 mg twice daily Cefuroxime (as axetil) (Zinacef®) (cefoxime axetil) oral therapy for 7 to 10 days.

Acute exacerbations of chronic bronchitis
750 mg Cefuroxime (as sodium) (Zinacef®) three times daily or twice daily (given i.v. or i.m.) for 48 to 72 hours, followed by 500 mg twice daily Cefuroxime (as axetil) (Zinacef®) (cefoxime axetil) oral therapy for 5 to 10 days.

RENAL IMPAIRMENT
Cefuroxime is excreted by the kidneys. Therefore, as with all such antibiotics, in patients with markedly impaired renal function it is recommended that the dosage of Cefuroxime (as sodium) (Zinacef®) should be reduced to compensate for its slower excretion. It is not necessary to reduce the standard dose (750 mg to 1.5 g three times daily) until the creatinine clearance falls to 20 ml/min or below.

In adults with marked impairment (creatinine clearance 10 to 20 ml/min) 750 mg twice daily is recommended and with severe impairment (creatinine clearance <10 ml/min) 750 mg once daily is adequate.

For patients on haemodialysis a further 750 mg dose should be given i.v. or i.m. at the end of each dialysis. In addition to parenteral use, Cefuroxime (as sodium) (Zinacef®) can be incorporated into the peritoneal dialysis fluid (usually 250 mg for every 2 litres of dialysis fluid).

For patients in renal failure on continuous arteriovenous haemodialysis or high-flux haemofiltration in intensive therapy units a suitable dosage is 750 mg twice daily. For low-flux haemofiltration follow the dosage recommended under impaired renal function.

CONTRAINDICATIONS
Hypersensitivity to cephalosporin antibiotics.

WARNINGS & PRECAUTIONS
Special care is indicated in patients who have experienced an allergic reaction to penicillins or other beta-lactams. Cephalosporin antibiotics at high dosage should be given with caution to patients receiving concurrent treatment with potent diuretics such as furosemide or aminoglycosides, as renal impairment has been reported with these combinations. Renal function should be monitored in these patients, the elderly, and those with pre-existing renal impairment (see Dosage and Administration). As with other therapeutic regimens used in the treatment of meningitis, mild-to-moderate hearing loss has been reported in a few paediatric patients treated with Cefuroxime (as sodium) (Zinacef®). Persistence of positive cerebral spinal fluid (CSF) cultures of Haemophilus influenzae at 18-36 hours has also been noted with Cefuroxime (as sodium) (Zinacef®) injection, as well as with other antibiotic therapies; however, the clinical relevance of this is unknown.

As with other antibiotics, use of Cefuroxime (as sodium) (Zinacef®) 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.

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.

Refer to the relevant prescribing information for Cefuroxime (as axetil) (Zinnat®) before initiating sequential therapy.

Effects on ability to drive and use machines
None reported.

DRUG INTERACTIONS
In common with other antibiotics, Cefuroxime (as sodium) (Zinacef®) may affect the gut flora, leading to lower oestrogen reabsorption and reduced efficacy of combined oral contraceptives.

Cefuroxime (as sodium) (Zinacef®) does not interfere in enzyme-based tests for glycosuria. Slight interference with copper reduction methods (Benedict’s, Fehling’s, Clinitest) may be observed. However, this should not lead to false-positive results, as may be experienced with some other cephalosporins.

It is recommended that either the glucose oxidase or hexokinase methods are used to determine blood/plasma glucose levels in patients receiving Cefuroxime (as sodium) (Zinacef®).

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 (as sodium) (Zinacef®), 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 Cefuroxime (as sodium) (Zinacef®) is administered to a nursing mother.

ADVERSE EFFECTS
Adverse drug reactions are very rare (<1/10,000) and 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 calculating incidence are not available. In addition the incidence of adverse reactions associated with Cefuroxime (as sodium) (Zinacef®) may vary according to the indication.

Data from clinical trials 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 a true frequency.

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
Rare Candida overgrowth

Blood and lymphatic system disorders
Common Neutropenia, eosinophilia.
Uncommon Leukopenia, decreased haemoglobin concentration, positive Coomb’s test.
Rare Thrombocytopenia.
Very rare Haemolytic anaemia.

Cephalosporins as a class tend to be absorbed onto the surface of red cell membranes and react with antibodies directed against the drug to produce a positive Coomb’s Test (which can interfere with cross matching of blood) and very rarely haemolytic anaemia.

Immune system disorders
Hypersensitivity reactions including
Uncommon Skin rash, urticaria and pruritus.
Rare Drug fever.
Very rare Interstitial nephritis, anaphylaxis, cutaneous vasculitis.
See also Skin and subcutaneous tissue disorders and Renal and urinary disorders.

Gastrointestinal disorders
Uncommon Gastrointestinal disturbance.
Very rare Pseudomembranous colitis (See Warnings and Precautions).

Hepatobiliary disorders
Common Transient rise in liver enzymes.
Uncommon Transient rise in bilirubin.

Transient rises in serum liver enzymes or bilirubin occur, particularly in patients with pre-existing liver disease, but there is no evidence of harm to the liver.
Skin and subcutaneous tissue disorders
Very rare  Erythema multiforme, toxic epidermal necrolysis and Stevens Johnson Syndrome.
See also Immune system disorders.

Renal and urinary disorders
Very rare  Elevations in serum creatinine, elevations in blood urea nitrogen and decreased creatinine clearance (See Warnings and Precautions).
See also Immune system disorders.

General disorders and administration site conditions
Common  Injection site reactions which may include pain and thrombophlebitis.
Pain at the intramuscular injection site is more likely at higher doses. However it is unlikely to be a cause for discontinuation of treatment.

OVERDOSAGE
Overdosage of cephalosporins can cause cerebral irritation leading to convulsions. Serum levels of cefuroxime can be reduced by haemodialysis or peritoneal dialysis.

STORAGE CONDITION
Store below 25°C. Protect from light. Some increase in the color of prepared solutions and suspensions of Cefuroxime (as sodium) (Zinacef®) may occur on storage. Reconstituted suspensions of Cefuroxime (as sodium) (Zinacef®) for intramuscular injection and aqueous solutions for direct intravenous injection retain their potency for 5 hours if kept below 25°C and for 48 hours if refrigerated.

INSTRUCTIONS FOR HANDLING

Intramuscular
Add 1 ml Water for Injections to 250 mg Cefuroxime (as sodium) (Zinacef®) or 3 ml Water for Injections to 750 mg Cefuroxime (as sodium) (Zinacef®). Shake gently to produce an opaque suspension.

Intravenous
Dissolve Cefuroxime (as sodium) (Zinacef®) in Water for Injections using at least 2 ml for 250 mg, at least 6 ml for 750 mg, or 15 ml for 1.5 g.

Intravenous infusion
Dissolve 1.5 g of Cefuroxime (as sodium) (Zinacef®) in 15 ml of Water for Injections. Add the reconstituted solution of Cefuroxime (as sodium) (Zinacef®) to 50 or 100 ml of a compatible infusion fluid (see information on Compatibility below). These solutions may be given directly into the vein or introduced into the tubing of the giving set if the patient is receiving parenteral fluids.

Incompatibilities
Cefuroxime (as sodium) (Zinacef®) should not be mixed in the syringe with aminoglycoside antibiotics.
The pH of 2.74% w/v Sodium Bicarbonate Injection BP considerably affects the colour of the solution and therefore this solution is not recommended for the dilution of Cefuroxime (as sodium) (Zinacef®). However, if required, for patients receiving Sodium Bicarbonate Injection by infusion Cefuroxime (as sodium) (Zinacef®) may be introduced into the tube of the giving set.

Compatibility
1.5g Cefuroxime (as sodium) (Zinacef®) constituted with 15ml Water for Injections may be added to metronidazole injection (500mg/100ml). 1.5 g Cefuroxime (as sodium) (Zinacef®) constituted with 15 ml Water for Injections may be added to metronidazole injection (500 mg/100 ml) and both retain their activity for up to 24 hours below 25°C.
1.5 g Cefuroxime (as sodium) (Zinacef®) is compatible with azlocillin 1 g (in 15 ml) or 5 g (in 50 ml) for up to 24 hours at 4°C or 6 hours below 25°C.
Cefuroxime (as sodium) (Zinacef®) [5 mg/ml] in 5% w/v or 10% w/v xylitol injection may be stored for up to 24 hours at 25°C.
Cefuroxime (as sodium) (Zinacef®) is compatible with aqueous solutions containing up to 1% lidocaine hydrochloride.
Cefuroxime (as sodium) (Zinacef®) is compatible with the more commonly used i.v. infusion fluids. It will retain potency for up to 24 hours at room temperature in:
- Sodium Chloride Injection BP 0.9% w/v
- 5% Dextrose Injection BP.
- 0.18% w/v Sodium Chloride plus 4% Dextrose Injection BP
- 5% Dextrose and 0.9% Sodium Chloride Injection
- 5% Dextrose and 0.45% Sodium Chloride Injection
- 5% Dextrose and 0.225% Sodium Chloride Injection
- 10% Dextrose Injection
- 10% Invert Sugar in Water for Injection
- Ringer's Injection USP
- Lactated Ringer's Injection USP
- M/6 Sodium Lactate Injection
- Compound Sodium Lactate Injection BP (Hartmann's Solution).

The stability of Cefuroxime (as sodium) (Zinacef®) in Sodium Chloride Injection BP 0.9% w/v and in 5% Dextrose Injection is not affected by the presence of hydrocortisone sodium phosphate.
Cefuroxime (as sodium) (Zinacef®) has also been found compatible for 24 hours at room temperature when admixed in i.v. infusion with: Heparin (10 and 50 units/ml) in 0.9% Sodium Chloride Injection; Potassium Chloride (10 and 40 mEq/L) in 0.9% Sodium Chloride Injection.
AVAILABILITY
Cefuroxime (as sodium) (Zinacef®) 250mg Powder for Injection: box of 1’s
Cefuroxime (as sodium) (Zinacef®) 750mg Powder for Injection: box of 1’s
Cefuroxime (as sodium) (Zinacef®) 1.5g Powder for Injection: box of 1’s

CAUTION
Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.
Keep all medicines out of reach of children.

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Version Number: GDS30/PI06. Revision Date: 09 August 2013

GlaxoSmithKline

Imported by:
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2286 Chino Roces Avenue, City of Makati
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Mfd by: GlaxoSmithKline Manufacturing S.p.A.
Verona, Italy
## Product Description

Cefuroxime axetil (Zinacef®) 250mg tablet: white, film-coated, capsule-shaped tablet engraved with ‘GXES7’ on one side and plain on the other. Each tablet contains 250mg Cefuroxime (as axetil).

Cefuroxime axetil (Zinacef®) 500mg tablet: white, film-coated, capsule-shaped tablet engraved with ‘GXEG2’ on one side and plain on the other. Each tablet contains 500mg Cefuroxime (as axetil).

## Pharmacologic 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.

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#### Commonly Susceptible Species

**Gram-Positive Aerobes:**
- *Streptococcus pyogenes*
- *Beta-hemolytic streptococci*

**Gram-Negative Aerobes:**
- *Haemophilus influenzae* including ampicillin resistant strains
- *Haemophilus parainfluenzae*
- *Moraxella catarrhalis*
- *Neisseria gonorrhoea* including penicillinase and non-penicillinase producing strains

**Gram-Positive Anaerobes:**
- *Peptostreptococcus spp.*
- *Propionibacterium spp.*

**Spirochetes:**
- *Borrelia burgdorferi*

#### Organisms for which acquired resistance may be a problem

**Gram-Positive Aerobes:**
- *Staphylococcus spp. including S. aureus (methicillin-susceptible isolates only)*
- *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. not including C. difficile*

**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*
### 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:
- Clostridium difficile

### Gram-Negative Anaerobes:
- Bacteroides fragilis

### Others:
- Chlamydia species
- Mycoplasma species
- Legionella species

### Pharmacokinetics

#### Absorption
After oral administration Cefuroxime axetil (Zinacef®) 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 Cefuroxime axetil (Zinacef®) tablets peak serum levels (2.9mg/l for a 125mg dose, 4.4mg/l for a 250mg dose, 7.7mg/l for a 500mg dose and 13.6mg/l for a 1g dose) occur approximately 2.4 hours after dosing when taken with food.

#### Distribution
Protein binding has been variously stated as 33 to 50% depending on the methodology used.

#### Metabolism
Cefuroxime is not metabolized.

#### 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.

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

### INDICATIONS
Cefuroxime axetil (Zinacef®) 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 Cefuroxime axetil (Zinacef®) will vary with geography and time and local susceptibility data should be consulted where available (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, 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 Cefuroxime axetil (Zinacef®) is effective when used following initial parenteral cefuroxime sodium (Zinacef®) 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).

Cefuroxime axetil (Zinacef®) should be taken after food for optimum absorption.

- Adults

<table>
<thead>
<tr>
<th>Condition</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most infections</td>
<td>250mg twice daily</td>
</tr>
<tr>
<td>Urinary tract infections</td>
<td>125mg twice daily</td>
</tr>
<tr>
<td>Mild to moderate lower respiratory tract infections e.g. bronchitis</td>
<td>250mg twice daily</td>
</tr>
<tr>
<td>More severe lower respiratory tract infections, or if pneumonia is suspected</td>
<td>500mg twice daily</td>
</tr>
<tr>
<td>Pyelonephritis</td>
<td>250mg twice daily</td>
</tr>
<tr>
<td>Uncomplicated gonorrhoe</td>
<td>single dose of 1g</td>
</tr>
<tr>
<td>Lyme disease in adults and children over the age of 12 years</td>
<td>500mg twice daily for 20 days</td>
</tr>
</tbody>
</table>

Sequential therapy

Pneumonia
1.5g cefuroxime sodium (Zinacef®) three times a day or twice a day (intravenous (i.v.) or intramuscular (i.m.)) for 48 to 72 hours, followed by Cefuroxime axetil (Zinacef®) oral therapy 500mg twice a day for 7 to 10 days.

Acute exacerbations of chronic bronchitis
750 mg cefuroxime sodium (Zinacef®) three times a day or twice a day (i.v. or i.m.) for 48 to 72 hours, followed by Cefuroxime axetil (Zinacef®) oral therapy 500mg 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

<table>
<thead>
<tr>
<th>Condition</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most infections</td>
<td>125mg (1 x 125mg tablet) twice daily, to a maximum of 250mg daily.</td>
</tr>
<tr>
<td>Children aged two years or older with otitis media or, where appropriate, with more severe infections</td>
<td>250mg (1 x 250mg tablet or 2 x 125mg tablets) twice daily, to a maximum of 500mg daily.</td>
</tr>
</tbody>
</table>

Cefuroxime axetil (Zinacef®) tablets should not be crushed and are therefore unsuitable for treatment of patients, such as younger children, who cannot swallow tablets. In children Cefuroxime axetil (Zinacef®) oral suspension may be used.

There is no experience of using Cefuroxime axetil (Zinacef®) in children under the age of 3 months.

- 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).

<table>
<thead>
<tr>
<th>Creatinine Clearance</th>
<th>T 1/2 (hours)</th>
<th>Recommended Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥30 mL/min</td>
<td>1.4 - 2.4</td>
<td>No dose adjustment necessary (standard dose of 125 mg to 500 mg given twice daily)</td>
</tr>
<tr>
<td>10-29 mL/min</td>
<td>4.6</td>
<td>Standard individual dose given every 24 hours</td>
</tr>
<tr>
<td>&lt;10 mL/min</td>
<td>16.8</td>
<td>Standard individual dose given every 48 hours</td>
</tr>
<tr>
<td>During haemodialysis</td>
<td>2 – 4</td>
<td>A single additional standard individual dose should be given at the end of each dialysis</td>
</tr>
</tbody>
</table>

CONTRAINDICATIONS

Patients with known hypersensitivity to cephalosporin antibiotics.

WARNINGS & 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 Cefuroxime axetil (Zinacef®) 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.

The Jarisch-Herxheimer reaction has been seen following Cefuroxime axetil (Zinacef®) treatment of Lyme disease. It results directly from the bactericidal activity of Cefuroxime axetil (Zinacef®) 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.

DRUG INTERACTIONS

Drugs which reduce gastric acidity may result in a lower bioavailability of Cefuroxime axetil (Zinacef®) 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 (Zinacef®) 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 (Zinacef®). This antibiotic does not interfere in the alkaline picrate assay for creatinine.

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.

PREGNANCY AND LACTATION

As this medicine may cause dizziness, patients should be warned to be cautious when driving or operating machinery.
There is no experimental evidence of embryopathic or teratogenic effects attributable to cefuroxime axetil 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 cefuroxime axetil is administered to a nursing mother.

ADVERSE EFFECTS

Adverse drug reactions to Cefuroxime axetil (Zinacef®) 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 (Zinacef®) 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.

**OVERDOSAGE**

**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.

**STORAGE CONDITION**

Cefuroxime axetil (Zinacef®) tablets should be stored at temperatures not exceeding 30°C. Protect from light.

**AVAILABILITY**

Cefuroxime axetil (Zinacef®) 250mg tablet: 10 tablets per double-foil blister (box of 50’s).

Cefuroxime axetil (Zinacef®) 500mg tablet: 10 tablets per double-foil blister (box of 50’s).

**CAUTION**

Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription. Keep all medicines out of reach of children.

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Version Number: GDS24/IPI04. Revision Date: 09 August 2013

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