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.

***In vitro* susceptibility of micro-organisms to Cefuroxime** Where clinical efficacy of cefuroxime has been demonstrated in clinical trials this is indicated with an asterisk (*).
Commonly Susceptible Species
Gram-Positive Aerobes: *Staphylococcus aureus (methicillin susceptible)** *Coagulase negative staphylococcus (methicillin susceptible)* *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 *Neisseria meningitidis* *Shigella* spp.
Gram-Positive Anaerobes: *Peptostreptococcus* spp. *Propionibacterium* spp.
Spirochetes: *Borrelia burgdorferi**
Organisms for which acquired resistance may be a problem
Gram-Positive Aerobes: *Streptococcus pneumoniae** Viridans group streptococcus
Gram-Negative Aerobes: *Bordetella pertussis* *Citrobacter* spp. not including *C. freundii* *Enterobacter* spp. not including *E. aerogenes* and *E. cloacae* *Escherichia coli** *Klebsiella* spp. including *K. pneumoniae** *Proteus mirabilis* *Proteus* spp. not including *P. penneri* and *P. vulgaris* *Providencia* spp. *Salmonella* 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 *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.

DOSAGE & 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) *(Zinnat®)* 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.

No more than 750 mg should be injected at one intramuscular site.

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) *(Zinnat®)*.

- **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) *(Zinnat®)* (cefuroxime axetil) oral therapy for 7 to10 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) *(Zinnat®)* (cefuroxime axetil) oral therapy for 5 to10 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) 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% lidoocaine 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 mEqL) 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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GlaxoSmithKline

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