

# NEW ZEALAND DATA SHEET

## 1. PRODUCT NAME

ZINACEF Cefuroxime sodium 750 mg powder for injection or infusion

ZINACEF Cefuroxime sodium 1.5 g powder for injection or infusion

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

ZINACEF injection contains either 750 mg, or 1.5 g of cefuroxime. Each 750 mg vial contains 42 mg sodium (1.8 mEq).

For full list of excipients, see Section 6.1 List of Excipients.

## 3. PHARMACEUTICAL FORM

Powder for injection/infusion.

Cefuroxime is a white to faintly yellow powder.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic Indications

Cefuroxime 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 sodium will vary with geography and time and local susceptibility data should be consulted where available (see Section 5.1 Pharmacodynamic properties).

### Indications include

- Respiratory tract infections for example, acute exacerbation of 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 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 (see Section 4.4 Special warnings and precautions for use).

Where appropriate ZINACEF is effective when used prior to oral therapy with ZINNAT (cefuroxime axetil) in the treatment of pneumonia and acute exacerbations of chronic bronchitis.

## **4.2 Dose and method of administration**

### Dose

ZINACEF Injection for intravenous (IV) and/or intramuscular (IM) administration only.

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

### **General Recommendations**

#### Adults

Many infections respond to 750 mg three times daily by intramuscular or intravenous injection. For more severe infections the dose should be increased to 1.5 g three times daily given intravenously. 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 (intravenously or intramuscularly) followed by oral therapy with 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 Section 5.2 Pharmacokinetic properties).

### **Gonorrhoea**

#### Adults

1.5 g as a single dose (as 2 x 750 mg injections given intramuscularly with different sites, e.g. each buttock).

### **Meningitis**

ZINACEF is suitable for sole therapy of bacterial meningitis due to sensitive strains.

#### Adults

3 g given intravenously every eight hours.

### Infants and Children

150 to 250 mg/kg/day given intravenously in 3 or 4 divided doses.

### Neonates

The dosage should be 100 mg/kg/day given intravenously.

## **Prophylaxis**

### Adults

The usual dose is 1.5 g given intravenously with induction of anaesthesia for abdominal, pelvic and orthopaedic operations. This may be supplemented with two 750 mg intramuscular doses eight and sixteen hours later.

In cardiac, pulmonary, oesophageal and vascular operations, the usual dose is 1.5 g given intravenously with induction of anaesthesia, continuing with 750 mg given intramuscularly three times daily for a further 24 to 48 hours.

In total joint replacement, 1.5 g cefuroxime 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 ZINACEF three times daily or twice daily (given intravenously or intramuscularly) for 48 to 72 hours, followed by 500 mg twice daily ZINNAT (cefuroxime axetil) oral therapy for 7 to 10 days.

Acute exacerbations of chronic bronchitis: 750 mg ZINACEF three times daily or twice daily (given intravenously or intramuscularly) for 48 to 72 hours, followed by 500 mg twice daily ZINNAT (cefuroxime axetil) oral therapy for 5 to 10 days.

### Special populations

## **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 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 intravenously or intramuscularly at the end of each dialysis. In addition to parenteral use, cefuroxime 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.

Cefuroxime is also available as the axetil ester (ZINNAT) for oral administration. This permits parenteral therapy with cefuroxime to be followed by oral therapy in situations where a change from parenteral to oral is clinically indicated.

#### Method of administration

For instructions on reconstitution of the medicine before administration, see Section 6.6 Special precautions for disposal and other handling.

### **4.3 Contraindications**

Hypersensitivity to cephalosporin antibiotics.

### **4.4 Special warnings and precautions for use**

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 Section 4.2 Dose and method of 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 sodium. Persistence of positive cerebral spinal fluid (CSF) cultures of *Haemophilus influenzae* at 18 to 36 hours has also been noted with cefuroxime sodium injection, as well as with other antibiotic therapies; however, the clinical relevance of this is unknown.

As with other antibiotics, use of cefuroxime may result in the overgrowth of *Candida*. Prolonged use may also result in the overgrowth of other non-

susceptible organisms (e.g. enterococci and *Clostridioides 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.

#### Intracameral use and ocular toxicity

Serious ocular toxicity, including corneal opacity, retinal toxicity and visual impairment has been reported following off-label intracameral use of ZINACEF. ZINACEF should not be administered intracamerally.

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 axetil before initiating sequential therapy.

#### **4.5 Interaction with other medicines and other forms of interaction**

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

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 ZINACEF.

This antibiotic does not interfere in the alkaline picrate assay for creatinine.

#### **4.6 Fertility, pregnancy and lactation**

##### Pregnancy

There is no experimental evidence of embryopathic or teratogenic effects attributable to cefuroxime, but, as with all medicines, it should be administered with caution during the early months of pregnancy.

##### Breast-feeding

Cefuroxime is excreted in human milk, and consequently caution should be exercised when ZINACEF is administered to a nursing mother.

### Fertility

There are no data on the effects of cefuroxime sodium on fertility in humans.

### **4.7 Effects on ability to drive and use machines**

No studies on the effects on the ability to drive and use machines have been performed. However, based on known adverse reactions, cefuroxime is unlikely to have an effect on the ability to drive and use machines.

### **4.8 Undesirable effects**

#### Summary of the safety profile

Adverse drug reactions are very rare (<1/10,000) and are generally mild and transient in nature.

#### Tabulated summary of adverse reactions

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 sodium 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 <1/10,000) 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  $\geq 1/10$ ,  
Common  $\geq 1/100$  to  $< 1/10$ ,  
Uncommon  $\geq 1/1000$  to  $< 1/100$ ,  
Rare  $\geq 1/10,000$  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.

### **Vascular disorders**

Common	Thrombophlebitis may follow intravenous injection.
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### **Gastrointestinal disorders**

Uncommon	Gastrointestinal disturbance.
Very rare	Pseudomembranous colitis (see Section 4.4 Special warnings and precautions for use).

### **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.
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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 Section 4.4 Special warnings and precautions for use).
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See also Immune system disorders.

### **General disorders and administration site conditions**

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

## Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions via: <https://nzphvc.otago.ac.nz/reporting/>

### **4.9 Overdose**

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

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

## **5. PHARMACOLOGICAL PROPERTIES**

### **5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: antibacterials for systemic use, second-generation cephalosporins, ATC code: J01DC02

#### Mechanism of Action

Cefuroxime is a well characterised and effective antibacterial agent which has bactericidal activity against a wide range of common pathogens, including  $\beta$ -lactamase producing strains.

Cefuroxime has good stability to bacterial  $\beta$ -lactamase, and consequently is active against many ampicillin-resistant or amoxicillin-resistant strains.

The bactericidal action of cefuroxime results from inhibition of cell wall synthesis by binding to essential target proteins.

#### Pharmacodynamic Effects

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
<b><u>Gram-Positive Aerobes:</u></b>
Staphylococcus aureus (methicillin susceptible)*



Coagulase negative staphylococcus (methicillin susceptible) Streptococcus pyogenes* Beta-hemolytic streptococci
<b><u>Gram-Negative Aerobes:</u></b> Haemophilus influenzae including ampicillin resistant strains* Haemophilus parainfluenzae* Moraxella catarrhalis* Neisseria gonorrhoea* including penicillinase and non-penicillinase producing strains Neisseria meningitidis Shigella spp.
<b><u>Gram-Positive Anaerobes:</u></b> Peptostreptococcus spp. Propionibacterium spp.
<b><u>Spirochetes:</u></b> Borrelia burgdorferi*
Organisms for which acquired resistance may be a problem
<b><u>Gram-Positive Aerobes:</u></b> Streptococcus pneumoniae* Viridans group streptococcus
<b><u>Gram-Negative Aerobes:</u></b> 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.
<b><u>Gram-Positive Anaerobes:</u></b> Clostridium spp.
<b><u>Gram-Negative Anaerobes:</u></b> Bacteroides spp. not including B. fragilis Fusobacterium spp.
Inherrently resistant organisms
<b><u>Gram-Positive Aerobes:</u></b> Enterococcus spp. including E. faecalis and E. faecium Listeria monocytogenes
<b><u>Gram-Negative Aerobes:</u></b> 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
<b><u>Gram-Positive Anaerobes:</u></b> Clostridioides difficile
<b><u>Gram-Negative Anaerobes:</u></b> Bacteroides fragilis
<b><u>Others:</u></b> Chlamydia species Mycoplasma species Legionella species

## 5.2 Pharmacokinetic properties

### Absorption

Peak levels of cefuroxime are achieved within 30 to 45 minutes after intramuscular administration.

### Distribution

Protein binding has been variously stated as 33 to 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.

### Biotransformation

Cefuroxime is not metabolised and is excreted by glomerular filtration and tubular secretion.

### Elimination

The serum half-life after either intramuscular or intravenous 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 (85-90%) of unchanged cefuroxime in urine within 24 hours of administration. The major part is excreted in the first six hours. Serum levels of cefuroxime are reduced by dialysis.

### **5.3 Preclinical safety data**

No additional data of relevance.

## **6. PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

None.

### **6.2 Incompatibilities**

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 ZINACEF. However, if required, for patients receiving Sodium Bicarbonate Injection by infusion the ZINACEF may be introduced into the tube of the giving set.

### **6.3 Shelf life**

Dry shelf life.

2 years at 25 °C.

Shelf life after reconstitution and dilution under controlled and validated aseptic conditions:

Suspension and solution for Injection - 5 hours below 25°C or 72 hours at 2 to 8°C.

Solution for Infusion - 3 hours below 25°C or 72 hours at 2 to 8°C.

Shelf life if reconstitution and dilution has not taken place in controlled and validated aseptic conditions:

ZINACEF should be used immediately or within 24 hours if stored at 2 to 8°C.

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

Store in original packaging to protect from light.

Some increase in the colour of prepared solutions and suspensions of ZINACEF may occur on storage.

For storage conditions after reconstitution of the medicine, see Section 6.3  
Shelf life

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

Vials (glass) containing 750 mg cefuroxime as the sodium salt (for use by intramuscular or intravenous injection) in packs of 5.

Vials (glass) containing 1.5 g cefuroxime as the sodium salt (for use by intravenous infusion), packed singly.

### **6.6 Special precautions for disposal and other handling**

Cefuroxime is a white to faintly yellow powder to which appropriate amounts of water are added to prepare an off-white suspension for intramuscular use or a yellow solution of intravenous administration. Variations in the intensity of this colour do not indicate any change in either the efficacy or safety of the product.

#### Instructions for reconstitution

##### Intramuscular

Add 3 mL Water for Injections to 750 mg ZINACEF. Shake gently to produce an off-white opaque suspension.

##### Intravenous

Dissolve ZINACEF in Water for Injections using at least 6 mL for 750mg, or at least 15 mL for 1.5 g. Shake gently to produce a yellowish solution.

##### Intravenous infusion

Dissolve 1.5 g of cefuroxime sodium in 15 ml of Water for Injections. Add the reconstituted solution of cefuroxime sodium to 50 or 100 ml of a compatible infusion fluid (see Compatibility). 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.

##### Compatibility

1.5 g ZINACEF constituted with 15mL Water for Injections may be added to metronidazole injection (500 mg/100 mL).

1.5 g ZINACEF is compatible with azlocillin 1 g (in 15 mL) or 5 g (in 50 mL).

ZINACEF (5 mg/mL) is compatible with 5% w/v or 10% w/v xylitol injection

ZINACEF may be constituted for IM use with aqueous solutions containing up to 1% lignocaine hydrochloride.

ZINACEF is compatible with the following more commonly used intravenous infusion fluids:

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 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.

ZINACEF has also been found compatible when admixed in intravenous 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.

Any unused medicine or waste material should be disposed of in accordance with local requirements.

## **7. MEDICINE SCHEDULE**

Prescription Medicine

## **8. SPONSOR**

GlaxoSmithKline NZ Limited  
Private Bag 106600  
Downtown Auckland  
NEW ZEALAND

Phone: (09) 367 2900  
Facsimile: (09) 367 2910

## **9. DATE OF FIRST APPROVAL**

Date of publication in the New Zealand Gazette of consent to distribute the medicine: 25 May 1979

## **10. DATE OF REVISION OF THE TEXT**

16 November 2020

Summary table of changes:

<b>Section changed</b>	<b>Summary of new information</b>
4.1	Replacement of the indication “acute and chronic bronchitis” with “acute exacerbation of chronic bronchitis”
4.4, 5.1	Replacement of 'Clostridium difficile' by 'Clostridioides difficile'

Version: 8.0

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