

NEW ZEALAND DATA SHEET

CEFUROXIME FOR INJECTION

Cefuroxime Sodium Injection Powder

250 mg, 500 mg & 1.5 g



Presentation

Cefuroxime for Injection vials contain 250mg, 750mg, or 1.5g of cefuroxime powder (as cefuroxime sodium) for injection or infusion.

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 for intravenous administration. Variations in the intensity of this colour do not indicate any change in either the efficacy or safety of the product.

Not all strengths may be marketed.

Uses

Actions

Bacteriology

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 amoxicillin-resistant strains.

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

Cefuroxime is usually active against the following organisms in vitro:

Aerobes Gram-negative

Escherichia coli.
Klebsiella spp.
Proteus mirabilis.
Providencia spp.
Proteus rettgeri.
Haemophilus influenzae (including ampicillin-resistant strains).
Haemophilus parainfluenzae (including ampicillin-resistant strains).
Moraxella (Branhamella) catarrhalis.
Neisseria gonorrhoeae (including penicillinase and non-penicillinase producing strains).
Neisseria meningitidis.
Salmonella spp.

Aerobes Gram-positive

Staphylococcus aureus and Staphylococcus epidermidis (including penicillinase producing strains but excluding methicillin resistant strains).
Streptococcus pyogenes (and other β -haemolytic streptococci).
Streptococcus pneumoniae.
Streptococcus Group B (Streptococcus agalactiae).
Streptococcus mitis (viridans group).
Bordetella pertussis.

Anaerobes

Gram-positive and Gram-negative cocci (including Peptococcus and Peptostreptococcus species).
Gram-positive bacilli (including most Clostridium species) and Gram-negative bacilli (including Bacteroides and Fusobacterium species).
Propionibacterium spp.

Other Organisms

Borrelia burgdorferi.

The following organisms are not susceptible to cefuroxime:

Clostridium difficile.
Pseudomonas spp.
Campylobacter spp.
Acinetobacter calcoaceticus.
Listeria monocytogenes.
Methicillin resistant strains of Staphylococcus aureus.
Methicillin resistant strains of Staphylococcus epidermidis.
Legionella spp.

Some strains of the following genera are not susceptible to cefuroxime:

Enterococcus (Streptococcus) faecalis.
Morganella morganii.
Proteus vulgaris.
Enterobacter spp.
Citrobacter spp.
Serratia spp.
Bacteroides fragilis.

In vitro the activities of cefuroxime and aminoglycoside antibiotics in combination have been shown to be at least additive with occasional evidence of synergy.

Pharmacokinetics

Peak levels of cefuroxime are achieved within 30 to 45 minutes after intramuscular administration. 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 3–5 times that in the adult.

Concurrent administration of probenecid prolongs the excretion of the antibiotic and produces an elevated peak serum level.

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

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.

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

Serum levels of cefuroxime are reduced by dialysis.

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.

Indications

Cefuroxime is a bactericidal cephalosporin antibiotic which is resistant to most β -lactamases and is active against a wide range of Gram-positive and Gram-negative organisms.

It is indicated for the treatment of infections before the infecting organism has been identified or when caused by sensitive bacteria.

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 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 **Pharmaceutical Precautions**).

Cefuroxime is also available as the axetil ester 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.

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

Dosage and Administration

Cefuroxime for Injection - for intravenous (IV) and/or intramuscular (IM) administration.

General Recommendations

Adults

Many infections respond to 750mg three times daily by intramuscular or intravenous injection. For more severe infections the dose should be increased to 1.5g three times daily given intravenously. The frequency of administration may be increased to 6-hourly if necessary, giving total daily doses of 3 to 6g. Where clinically indicated, some infections respond to 750mg or 1.5g twice daily (intravenously or intramuscularly) followed by oral therapy with cefuroxime axetil.

Infants and Children

30 – 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 – 100 mg/kg/day given as 2 or 3 divided doses (see **Pharmacokinetics**).

Gonorrhoea

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

Meningitis

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

Adults

3g given intravenously every eight hours.

Infants and Children

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

Neonates

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

Prophylaxis

The usual dose is 1.5g given intravenously with induction of anaesthesia for abdominal, pelvic and orthopaedic operations. This may be supplemented with two 750mg intramuscular doses 8 and 16 hours later.

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

In total joint replacement, 1.5g cefuroxime powder may be mixed dry with each pack of methyl methacrylate cement polymer before adding the liquid monomer.

Sequential Therapy

Pneumonia

1.5g cefuroxime three times daily or twice daily (given intravenously or intramuscularly) for 48-72 hours, followed by 500mg twice daily cefuroxime axetil oral therapy for 7-10 days.

Acute Exacerbations of Chronic Bronchitis

750mg cefuroxime three times daily or twice daily (given intravenously or intramuscularly) for 48-72 hours, followed by 500mg twice daily cefuroxime axetil oral therapy for 5-10 days.

Duration of both parenteral and oral therapy is determined by the severity of the infection and the clinical status of the patient.

Impaired Renal Function

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 should be reduced to compensate for its slower excretion.

It is not necessary to reduce the standard dose (750mg – 1.5g three times daily) until the creatinine clearance falls to 20 mL/min or below.

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

For patients on haemodialysis a further 750mg 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 250mg 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 750mg twice daily. For low-flux haemofiltration follow the dosage recommended under Impaired Renal Function.

Cefuroxime is also available as the axetil ester 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.

Administration

Preparation of a Suspension for Intramuscular Injection

Add 1ml Water for Injections to 250mg Cefuroxime for Injection or 3ml Water for Injections to 750mg Cefuroxime for Injection. Shake gently to produce an opaque suspension.

Preparation of a Solution for Intravenous Injection

250mg & 750mg Vials

For reconstitution of the powder dissolve Cefuroxime for Injection in Water for Injections using at least 2ml for 250mg and at least 6ml for 750mg.

1.5g Vial

For reconstitution of the powder

Draw up at least 15ml of water for injections into a suitable syringe (20ml).
Transfer 10ml into the 1.5g vial and reconstitute the contents of the vial.
Then draw up the dissolved contents of the vial into the same syringe.

Preparation of a Solution for Intravenous Infusion

1.5g Vial

For intravenous infusions of less than 30 minutes, the contents of the 1.5 g vial may be dissolved in a 50 ml vial or bag of Water for Injection as follows:

For reconstitution of the powder

Draw up at least 10ml of water for injections from the 50ml vial or bag using a suitable syringe.
Transfer the 10ml into the 1.5g vial and reconstitute the content of the vial.
Then transfer the dissolved contents of the vial into the 50ml vial or bag.

The solution may be administered directly into the vein or introduced into the tubing of the giving set if the patient is receiving parenteral fluid.

Contraindications

Hypersensitivity to cephalosporin antibiotics.

Warnings and Precautions

Special care is indicated in patients who have experienced an allergic reaction to penicillins or other beta-lactams.

Cephalosporin antibiotics at high dosage should be given with caution to patients receiving concurrent treatment with potent diuretics such as frusemide 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 sodium. Persistence of positive CSF cultures of *Haemophilus influenzae* at 18-36 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 *Clostridium difficile*), which may require interruption of treatment.

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 axetil before initiating sequential therapy.

Pregnancy and Lactation

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

Effects on Ability to Drive and Operate Machinery

None reported.

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 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 <1/1000) 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 and < 1/10,
Uncommon	≥ 1/1000 and < 1/100,
Rare	≥ 1/10,000 and < 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 **Adverse Effects - Skin and Subcutaneous Tissue Disorders** and **Adverse Effects - Renal and Urinary Disorders**.

Vascular Disorders

Common: Thrombophlebitis may follow intravenous injection.

Gastrointestinal Disorders

Uncommon: Gastrointestinal disturbance.

Very rare: Pseudomembranous colitis.

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 **Adverse Effects - 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 **Adverse Effects - Immune system disorders**.

General Disorders and Administration Site Conditions

Rare: Transient pain at injection site.

Pain at the intramuscular injection site is more likely at higher doses. However it is unlikely to be a cause for discontinuation of treatment.

Interactions

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

Cefuroxime 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.

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

See also **Pharmaceutical Precautions – Compatibilities** and **Pharmaceutical Precautions – Incompatibilities**.

Overdosage

Overdosage of cephalosporins can cause cerebral irritation leading to convulsions.

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

Pharmaceutical Precautions

Store below 25°C. Protect from light.

Reconstituted Cefuroxime

Suspensions of cefuroxime for intramuscular injection and aqueous solutions for direct intravenous injection retain their potency for five hours if kept below 25°C and for 24 hours if refrigerated.

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

Incompatibilities

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

Compatibilities

1.5g cefuroxime 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.

1.5g cefuroxime is compatible with azlocillin 1g (in 15mL) or 5g (in 50mL) for up to 24 hours at 4°C, or 6 hours below 25°C.

Cefuroxime (5mg/mL) in 5%w/v or 10%w/v Xylitol Injection may be stored for up to 24 hours at 25°C.

Cefuroxime is compatible with aqueous solutions containing up to 1% lignocaine hydrochloride.

Cefuroxime is compatible with the following more commonly used intravenous 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 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 has also been found compatible for 24 hours at room temperature 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.

Medicine Classification

Prescription Medicine.

Package Quantities

Vials containing 250mg or 750mg cefuroxime as the sodium salt (for use by intramuscular or intravenous injection) are available in packs of 5.

Vials containing 1.5g cefuroxime as the sodium salt (for use by intravenous infusion) are packed individually.

Not all strengths may be marketed.

Further Information

Nil.

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