

Cefuroxime-AFT

Cefuroxime sodium equivalent to Cefuroxime 250 mg, 750 mg and 1.5 g Powder for Injection

Presentation

CEFUROXIME-AFT 250 mg contains Cefuroxime sodium equivalent to Cefuroxime 250 mg.

CEFUROXIME-AFT 750 mg contains Cefuroxime sodium equivalent to Cefuroxime 750 mg.

CEFUROXIME-AFT 1.5 g contains Cefuroxime sodium equivalent to Cefuroxime 1.5 g.

Cefuroxime sodium is a white to off-white powder which when reconstituted with appropriate amounts of water provides either an off-white suspension for intramuscular (I.M) use or a yellow solution for intravenous (I.V.) use. Variations in colour intensity do not indicate any change in the product safety or efficacy.

Uses

Actions

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.

Salmonellae 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.

CEFUROXIME-AFT 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 e.g. acute and chronic bronchitis, infected bronchiectasis, bacterial pneumonia, lung abscess and post-operative chest infections.
- Ear, nose and throat infections e.g. sinusitis, tonsillitis, pharyngitis and otitis media.
- Urinary tract infections e.g. acute and chronic pyelonephritis, cystitis and asymptomatic bacteriuria.
- Soft-tissue infections e.g. cellulitis, erysipelas and wound infections.
- Bone and joint infections e.g. 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-AFT will be effective alone, but when appropriate it may be used in combination with an aminoglycoside antibiotic, or in conjunction with metronidazole, especially for prophylaxis in colonic or gynaecological surgery. Where appropriate, CEFUROXIME-AFT 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-AFT Injection can be used for I.V. and/or I.M. administration.

Preparation for I.M. Administration

CEFUROXIME-AFT 250 mg and 750 mg vials are intended for I.M. administration. Add into the vial, 1 mL of Water for Injections to the 250 mg strength or 3 mL of Water for Injections to the 750 mg strength. Shake well to obtain a suspension. While it is recommended that freshly prepared suspensions are used, the suspension may be stored under refrigeration (2-8 °C) for up to 24 hours.

Preparation for I.V. Administration

Add 2 mL, 6 mL and 15 mL of Water for Injections to the 250 mg, 750 mg and 1.5 g vials respectively. Shake well to obtain a clear solution. While it is recommended that freshly prepared solutions are used, the solution may be stored under refrigeration (2-8 °C) for up to 24 hours.

The reconstituted solution (normally 1.5 g in 15 mL) can be further diluted for use as a I.V. infusion by adding to 50 or 100 mL of a compatible infusion solution. 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.

General 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 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.

Gonorrhoea:

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

Meningitis:

CEFUROXIME-AFT is suitable for sole therapy of bacterial meningitis due to sensitive strains.

Adults:

3 g 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 1.5 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 eight and sixteen 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 powder may be mixed dry with each pack of methyl methacrylate cement polymer before adding the liquid monomer.

Sequential therapy:**Pneumonia:**

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

Acute exacerbations of chronic bronchitis:

750 mg three times daily or twice daily (I.M. or I.V.) for 48-72 hours, followed by 500 mg 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. In patients with markedly impaired renal function it is recommended that the dosage should be reduced to compensate for its slower excretion.

It is not necessary to reduce the standard dose (750 mg - 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 – 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 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.

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.

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.

Use during 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 administered to a nursing mother.

Effects on ability to drive and use machines

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 $\geq 1/10$,

common $\geq 1/100$ and $<1/10$,

uncommon $\geq 1/1000$ and $<1/100$,

rare $\geq 1/10,000$ 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 Skin and subcutaneous tissue disorders and Renal and urinary disorders.

Vascular disorders

Common: Thrombophlebitis may follow I.V. 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 Immune system disorders.

Renal and urinary disorders

Very rare: Elevations in serum creatinine, elevations in blood urea nitrogen and decreased creatinine clearance.

See also 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. Ceuroxime does not interfere in the alkaline picrate assay for creatinine.

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.

It is recommended that the reconstituted suspensions or solutions be used immediately after preparation but they are stable for up to 24 hours when stored in the refrigerator.

Compatibility

1.5 g CEFUROXIME-AFT reconstituted with 15 mL Water for Injections may be added to metronidazole injection (500 mg/100 mL) with both retaining their activity for up to 24 hours when stored below 25°C.

1.5 g CEFUROXIME-AFT is compatible with azlocillin 1 g (in 15 mL) or 5 g (in 50 mL) for up to 24 hours under refrigeration (2-8 °C) or for 6 hours below 25°C.

CEFUROXIME-AFT (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-AFT is compatible with aqueous solutions containing up to 1% lignocaine hydrochloride.

CEFUROXIME-AFT is compatible with the 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-AFT 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-AFT has 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 40mEqL) in 0.9% Sodium Chloride Injection.

Medicines Classification

Prescription Only Medicine

Package Quantities

Cefuroxime-AFT 250 mg, 750 mg and 1.5 g are available in packs containing 1 and 10 vials.

Further Information

Sodium content is as follows:

Each 250 mg vial contains 14 mg sodium (5 mEq), each 750 mg vial contains 42 mg sodium (1.8 mEq) and each 1.5 g vial contains 84 mg sodium (3.6 mEq).

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