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Cefuroxime Vit

Active substance: Cefuroxime 750 mg (as Cefuroxime sodium).

Powder for Solution or suspension for Injection or infusion IM/IV
Cefuroxime is a white or almost white powder to which appropriate amounts of water are added.

Sodium content per vial: 41.4 mg.

Indications

Infections caused by susceptible microorganisms, prophylaxis against post operative infections in a variety of operations.

Uses

Actions

Cefuroxime has bactericidal activity against a wide range of common pathogens, including beta-lactamaseproducing strains. It is indicated for the treatment of infections before the infecting organism has been identified or when caused by sensitive bacteria. In addition, it is effective prophylactic against post-operative infection in a variety of operations. 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 gynecological surgery (see *Pharmaceutical Precautions*).

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

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

Cefuroxime is usually active against the following organisms *in vitro*:

Aerobes Gram-Negative

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

Aerobes Gram-Positive

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

Anaerobes

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

Other organisms
Borrelia burgdorferi.

The following organisms are not susceptible to cefuroxime: *Clostridium difficile, Pseudomonas* spp., *Acinetobacter calcoaceticus, Listeria monocytogenes,* methicillin-resistant strains of *Staphylococcus aureus,* methicillin-resistant strains of *Staphylococcus epidermis,* and *Legionella* spp.

Some strains of the following genera are not susceptible to cefuroxime: *Enterococcus (Streptococcus) faecalis, Morganella morganii, Proteus vulgaris, Enterobacter* spp., *Serratia* spp., and *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.

Pharmacotherapeutic Group:
Antibacterials/ Cephalosporins

ATC code: J01DC02

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. 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 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 metabolized 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 humor. Cefuroxime passes the blood-brain barrier when the meninges are inflamed.

Dosage and Administration

GENERAL DOSAGE RECOMMENDATIONS

Adults
Many infections will respond to 750 mg three times daily by IM or IV injection. For more severe infections, this dose should be increased to 1.5 g three times daily. IV. The frequency of IM or IV injections can be increased to six-hourly if necessary, giving total doses of 3 g to 6 g daily.

Infants and Children
Doses of 30 to 100 mg/kg/day given as three or four divided doses. A dose of 60 mg/kg/day will be appropriate for most infections.

Neonates
Doses of 30 to 100 mg/kg/day given as two or three divided doses. In the first weeks of life the serum half-life of cefuroxime can be three to five times that in adults.

OTHER RECOMMENDATIONS

Gonorrhoea
1.5 g should be given as a single dose. This may be given as 2x750 mg injections (intramuscularly) into different sites, e.g. each buttock.

Meningitis

Cefuroxime is suitable for sole therapy of bacterial meningitis due to sensitive strains. The following doses are recommended:

Infants and Children
200 to 240 mg/kg/day IV in three or four divided doses. This dosage may be reduced to 100 mg/kg/day IV after three days or when clinical improvement occurs.

Neonates
The initial dosage should be 100 mg/kg/day IV. A reduction to 50 mg/kg/day IV may be made when clinically indicated.

Adults
3 g IV every eight hours. Data are not yet sufficient to recommend a dose for intrathecal administration.

Prophylaxis
The usual dose is 1.5 g IV with induction of anaesthesia for abdominal, pelvic and orthopedic operations, but may be supplemented with two 750 mg IM doses 8 and 16 hours later. In cardiac, pulmonary, oesophageal and vascular operations, the usual dose is 1.5 g IV with induction of anaesthesia continuing with 750 mg IM 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.

Dosage in 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. However, 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 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 IV or IM 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 given IV.

Dosage in Continuous Arteriovenous Haemodialysis (CAVHD) or Haemofiltration (CAVH)
For patients in renal failure on continuous arteriovenous haemodialysis or highflux haemofiltration in intensive therapy units a suitable dosage is 750 mg twice daily. For low-flux haemofiltration follow the dosage recommended under *Dosage in Impaired Renal Function*.

ADMINISTRATION

Intramuscular injection
Add 3 ml Water for Injections to 750 mg cefuroxime. Shake gently to produce an opaque suspension.

Intravenous
Intravenous injection: Dissolve cefuroxime in Water for Injections using 6 ml for 750 mg.
Intravenous infusion: Cefuroxime is compatible with the most commonly used intravenous fluids.
Dissolve Cefuroxime 750 mg in at least 25 ml of:
NaCl 0.9%
Dextrose 10%
M/6 Sodium Lactate for Injection
Ringer Lactate
Ringer for Injection

Dextrose 5%
Dextrose 5% containing 0.9%, 0.45% and 0.225% NaCl
Dextrose 5% containing 20 mEq KCl
Heparin (10 and 50 units/ml) in 0.9% NaCl 10 and 40 mEq KCl in 0.9% NaCl
Dextrose 4% containing 0.18% NaCl
10% Invert Sugar in Water for Injections
Hartmann's 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.

Contraindications

Cefuroxime is contraindicated in patients with hypersensitivity to the active substance or any cephalosporin antibiotics.

Warnings and Precautions

This product should not ordinarily be given to those known to be allergic to penicillin or to cephalosporins, especially if they have experienced an allergic or urticarial reaction. 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 falsepositive 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.

Pseudomembranous colitis has been associated with the use of cefuroxime and may occur during or after treatment.

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.

Adverse Effects

Adverse reactions to cefuroxime have occurred relatively infrequently and have been generally mild and transient in nature.

Hypersensitivity reactions have been rarely reported; these include skin rashes, urticaria, pruritus, interstitial nephritis, medicine fever and very rarely anaphylaxis, polymorphous erythema and on very exceptional occasions the the Stevens-Johnson syndrome, the Lyell's syndrome. As with other antibiotics, prolonged use may result in the overgrowth of non-susceptible organisms, e.g. *Candida.* Gastrointestinal disturbance, including, very rarely, symptoms of pseudomembranous colitis during or after treatment.

As with other therapeutic regimens used in the treatment of meningitis, mild-to-moderate hearing loss has been reported in a few pediatric 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. The correlation between delayed CSF sterilization and subsequent hearing impairment has not been fully established and the clinical relevance is unknown.

The principal changes in haematological parameters seen in some patients have been decreased haemoglobin concentration and eosinophilia, leukopenia and neutropenia. A positive Coombs' test has been found in some patients treated with cefuroxime - this phenomenon can interfere with the cross-matching of blood. Although there are sometimes transient rises in serum liver enzymes or serum bilirubin, particularly in patients with pre-existing liver disease, there is no evidence of harm to the liver.

Elevations in serum creatinine and/or blood urea nitrogen and a decreased creatinine clearance have been observed (see *Warnings and Precautions*).

Transient pain may be experienced at the site of intramuscular injection. This is more likely to occur with higher doses. However, it is unlikely to be a cause for discontinuation of treatment.

Occasionally thrombophlebitis may follow intravenous injection.

Administering high doses of betalactams, especially to patients suffering from renal failure may lead to metabolic encephalopathies (consciousness disorders, abnormal motions, and convulsive crises).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.

Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form
http://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il

Interactions

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

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*).

Cefuroxime 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.

Storage

Do not store above 25°C. Keep the vial in the outer carton in order to protect from light.

Cefuroxime should not be mixed in the same syringe or in the same infusion bag with aminoglycoside antibiotics.

Cefuroxime should not be mixed with solutions with pH above 7,5, i.e. sodium hydrogen carbonate.

Shelf life

The expiry date of the product is indicated on the packaging materials.

Shelf life after reconstitution:
Chemical and physical stability has been demonstrated for 8 hours at 25ºC and 48 hours at 2-8ºC.

Shelf life after dilution:
Chemical and physical stability has been demonstrated for 12 hours at 25ºC and 48 hours at 2-8ºC.

From a microbiological point of view the reconstituted solution should be used immediately. If reconstituted product is not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 – 8 °C unless the preparation has taken place under controlled and validated aseptic conditions.

Presentation
Cefuroxime Vit – 10 vials

Registration Number

Manufacturer
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