ZINEX

Vial

Composition

Each vial contains 750 mg of Cefuroxime (as Sodium).

Action

Cefuroxime is a well-characterized and effective antibacterial agent that 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.

Cefuroxime is usually active against the following organisms:

Aerobes Gram-negative

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

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)

Anaerobes

- Gram-positive and Gram-negative cocci (including Peptococcus and Peptostreptococcus species)
- Gram-positive bacilli (including 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 and 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.*

Pharmacokinetics

Peak serum levels of Cefuroxime are reached 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 produces an elevated peak serum level and restricts the excretion of the antibiotic. There is almost complete recovery of unchanged Cefuroxime in the urine within 24 hours of administration the major part being eliminated within the first 6 hours. The tubular excretion component of renal clearance of Cefuroxime is of the order of 50%.

Indications

Zinex is indicated for the treatment of infections caused by susceptible strains of the designated microorganisms in the diseases listed below:

- Respiratory tract infections
- Ear, nose and throat infections
- Urinary tract infections
- Bone and joint infections
- Soft tissue infections
- Obstetrics and gynecological infections
- Gonorrhea
- Prophylaxis against infection in abdominal, cardiac, and pulmonary surgery where there is an increased risk of infection.

Contraindications

Cefuroxime, is contraindicated in patients with known allergy to the cephalosporins group of antibiotics.

Warnings

Before therapy with Sterile Cefuroxime sodium, careful inquiry should be made to determine whether the patient has had previous hypersensitivity reactions to cephalosporins, penicillins, or other drugs. This product should be given cautiously to penicillin-sensitive patients.

Antibiotics should be administered with caution to any patient who has demonstrated some form of allergy, particularly to drugs. If an allergic reaction to Cefuroxime occurs, discontinue the drug.

Serious acute hypersensitivity reactions may require epinephrine and other emergency measures Pseudomembranous colitis has been reported with the use of cephalosporins (and other broad-spectrum antibiotics); therefore, it is important to consider its diagnosis in patients who develop diarrhea in association with antibiotic use. Treatment with broad-spectrum antibiotics alters normal flora of the colon and may permit overgrowth of clostridia. Studies indicate a toxin produced by C. difficile is one primary cause of antibiotic-associated colitis. Cholestyramine and colestipol resins have been shown to bind the toxin in vitro.

Mild cases of colitis may respond to drug discontinuance alone. Moderate to severe cases should be managed with fluid, electrolyte, and protein supplementation as indicated. When the colitis is not relieved by drug discontinuance or when it is severe, oral vancomycin is the treatment of choice for antibiotic-associated pseudomernbranous colitis produced by C. difficile. Other causes of colitis should also be considered.

Adverse Reactions

Thrombophlebitis after intravenous injection, gastrointestinal disturbance including diarrhea, nausea, and vomiting and *Candida intertrigo* has been reported.
Hypersensitivity reactions such as skin rashes (maculopapular and urticarial), drug fever reactions resembling serum sickness and anaphylaxis have been reported. There have also been reports of erythema multiforme including the Stevens - Johnson syndrome, and toxic epidermal necrolysis.
The main changes in hematological parameters seen in some patients have been the unexplained decreased hemoglobin concentration and eosinophilia.

Patients developing eosinophilia should have renal function closely monitored, since hypersensitivity with acute renal failure has previously been documented.
Leucopenia, neutropenia, and thrombocytopenia been noted.
Patients developing decreased hemoglobin concentration should have their bone marrow response monitored.

A positive Coombs test has been found with patients treated with Cefuroxime, which can interfere with the cross matching of blood. Hemolytic anaemia may occur.
There are sometimes rises in serum liver enzymes or serum bilirubin, particularly in patients with pre-existing liver disease. These have usually returned to normal when therapy has stopped with no ill effect.

There may also be some variation in the results of biochemical tests of renal function, but these do not appear to be of clinical importance. If renal function is already impaired, this should be monitored as a precaution.
Transient pain may be experienced at the site of intramuscular injection, which is more likely to occur with higher doses. However, it is unlikely to be a cause for discontinuation of the treatment.

Precautions

General

Although Cefuroxime rarely produces alterations in kidney function, evaluation of renal status during therapy is recommended, especially in seriously ill patients receiving the maximum doses.
Cephalosporins should be given with caution to patients receiving concurrent treatment with potent diuretics as these regimens are suspected of adversely affecting renal function. The total daily dose of Cefuroxime should be reduced in patients with transient or persistent renal insufficiency because high and prolonged serum antibiotic concentrations can occur in such individuals front usual doses.

As with other antibiotics, prolonged use of Cefuroxime may result in overgrowth of nonsusceptible organisms. Careful observation of the patient is essential. If super infection does occur during therapy, appropriate measures should be taken.

Broad-spectrum antibiotics should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis. Nephrotoxicity has been reported following concomitant administration of aminoglycoside antibiotics and cephalosporins.

Interference with Laboratory Tests

A false-positive reaction for glucose in the urine may occur with copper reduction tests (Benedict's or Fehling's solution or with Clinitest tablets), but not with enzyme-based tests for glycosuria (e.g., Testape). A false negative reaction may occur in the ferricyanide test for blood glucose.
Cefuroxime does not interfere with the assay of serum and urine creatinine by the alkaline pierate method.

Pregnancy

Category B
There are no adequate, well-controlled studies in pregnant women. This drug should be used during pregnancy only if clearly needed.

Nursing Mothers

Since Cefuroxime is excreted in human milk, caution should be exercised when Cefuroxime is administered to a nursing woman.

Pediatric Use
Safety and effectiveness in children below the age of 3 months have not been established. Accumulation of other members of the cephalosporin class in newborn infants (with resulting prolongation of drug half-life) has been reported.

Dosage and Administration

General dosage recommendation
Adults
the dosage range for adults lies between 1.5 g to 6 g/day. Many infections will respond to 750 mg 3 times daily given by intramuscular or intravenous injection. For more severe infections, this dose should be increased to 1.5 g 3 times daily intravenously. The frequency of intramuscular or intravenous injection can be increased to 6-hourly if necessary.

Infants and children
Doses of 30 to 100 mg/kg/day given as 3 to 4 divided doses. A dose of 60 mg/kg/day will be appropriate for most infections.

Other recommendations
Gonorrhea
1.5 g Zinex should be given as a single dose. This may be given as 2 x 750 mg injections into different sites, e.g. into each buttock.

Surgical Infection Prophylaxis
The usual dose is 1.5 g intravenously with induction of anesthesia for abdominal and gynecological operations but this may be supplemented with 2 x 750 mg intramuscular doses 8 and 16 hours later. In cardiac and pulmonary operations, the usual dose is 1.5 g intravenously with induction of anesthesia continuing with 750 mg intramuscularly 3 times daily for a further 24 to 48 hours.

Dosage in impaired renal function
Zinex is excreted by the kidneys. Therefore, in patients with markedly impaired renal function, it is recommended that the dosage of Zinex should be reduced to compensate for its slower excretion. However, it is not necessary to reduce the dose until the Glomerular Filtration Rate falls below 20 ml/min. In adults with marked impairment (Glomerular Filtration Rate 10 to 20 ml/min) 750 mg twice daily is recommended and with severe impairment (Glomerular Filtration Rate less than 10 ml/min), 750 mg once daily is adequate. For patients on dialysis, a further 750 mg dose should be given at the end of each dialysis. When continuous peritoneal dialysis is being used, a suitable dosage is usually 750 mg twice daily. In the treatment of beta-hemolytic streptococcal infections, a therapeutic dose must be administered for at least 10 days.

Zinex is compatible with the more commonly used intravenous fluids. It will retain its potency for up to 24 hours at room temperature (25°C) or seven days under refrigeration in 0,9% m/v Sodium Chloride injection BP, 5% Dextrose injection BP 0,18% m/v Sodium Chloride plus 4% Dextrose injection BP and Compound Sodium Lactate injection BP (Hartmann's solution). The pH of 2,74% m/v Sodium Bicarbonate injection B.P. 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 by infusion the Zinex may be introduced into the tube of the administration set. The stability of Zinex in 0.9% m/v Sodium Chloride injection BP and in 5% Dextrose injection is not affected by the presence of hydrocortisone sodium phosphate. Zinex is also compatible with aqueous solution containing up to 1% lignocaine HCl. Darkening of the powder or solution does not affect the potency.

Over Dosage

Signs and Symptoms

Experience with overdose of Cefuroxime sodium in humans is limited. The administration of inappropriately large doses of parenteral cephalosporins may cause seizures, particularly in patients with renal failure in whom accumulation is likely to occur.

In managing over dosage, consider the possibility of multiple drug overdoses, interaction among drugs, and unusual drug kinetics in your patient.

Protect the patient's airway and support ventilation and perfusion. Meticulously monitor and maintain, within acceptable limits, the patient's vital signs, blood gases, serum electrolytes, etc. If the patient develops convulsions, the drug should be promptly discontinued; anticonvulsant therapy may be administered if clinically indicated. The use of hemodialysis in the treatment of Cefuroxime overdose has not been established.

Presentation

Box of one vial