110x193mm

FRONT

For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only

ZEFONE-1000
CEFTRIAXONE FOR INJECTION USP

COMPOSITION :
Each vial of Zefone 1000 contains :
Ceftriaxone sodium U.S.P.
equivalent to Ceftriaxone 1000 mg

CLINICAL PHARMACOLOGY :
The bactericidal activity of Ceftriaxone results from inhibition of cell wall synthesis. Ceftriaxone has a high degree of stability in the presence of beta-lactamases, both penicillanases and cephalosporinases of gram-negative and positive bacteria. Ceftriaxone is usually active against the following microorganisms in vitro and in clinical infections:

Gram-Negative Aerobes : *Acinetobacter calcoaceticus, Enterobacter aerogenes, Enterobacter cloacae, Escherichia coli, Haemophilus influenzae* (including ampicillin resistant and beta-lactamase producing strains), *Haemophilus parainfluenzae, Klebsiella oxytoca, Klebsiella pneumoniae, Moraxella catarrhalis* (including beta-lactamase producing strains), *Morganella morganii, Neisseria gonorrhoeae* (including penicillinase and nonpenicillinase-producing strains), *Neisseria meningitidis, Proteus mirabilis, Proteus vulgaris, and Serratia marcescens.* Ceftriaxone is also active against many strains of *Pseudomonas aeruginosa.*

NOTE: Many strains of the above organisms that are multiply resistant to other antibiotics, eg, penicillins, cephalosporins and aminoglycosides, are susceptible to Ceftriaxone.

Gram-Positive Aerobes : *Staphylococcus aureus* (including penicillinase-producing strains), *Staphylococcus epidermidis, Streptococcus pneumoniae, Streptococcus pyogenes, Viridans group streptococci.*

NOTE: Methicillin-resistant staphylococci are resistant to cephalosporins, including Ceftriaxone. Most strains of Group D streptococci and enterococci, e.g.,*Enterococcus (Streptococcus) faecalis are resistant.*

Anaerobes : *Bacteroides fragilis, Clostridium* species and *Peptostreptococcus species.*

NOTE: Most strains of *C. difficile* are resistant. Ceftriaxone also demonstrates *in vitro* activity against most strains of the following microorganisms, although the clinical significance is unknown:

Gram-Negative Aerobes :- *Citrobacter diversus, Citrobacter freundii, Providencia* species (including *Providencia rettgeri), Salmonella* species (including *S.typhi),* and *Shigella* species,

Gram-*Positive Aerobes :* *Streptococcus* agalactiae. **Anaerobes:** *Bacteroides bivius, and Bacteroides melaninogenicus.*

PHARMACOKINETICS :
Ceftriaxone is administered by injection as the sodium salt. After intramuscular injection mean peak plasma concentrations of about 43 and 80 mcg/ml have been reported about 2 hours after the equivalent of 0.5 and 1 gm of Ceftriaxone respectively. Ceftriaxone demonstrates non-linear, dose-dependent pharmacokinetics. This is due to binding to plasma proteins which varies from 85 to 95% in a dose-dependent manner. The elimination half-life of Ceftriaxone is not dependent on the dose and varies between 6 and 9 hours; it is prolonged in neonates.

Ceftriaxone is widely distributed in body tissues and fluids; therapeutic concentrations have been achieved in the cerebrospinal fluid when the meninges are inflamed. It diffuses across the placenta and is excreted in the breast milk in low concentrations.

About 45 to 65% of a dose of Ceftriaxone is excreted unchanged in the urine, principally by glomerular filtration; the remainder is excreted in the bile and is ultimately found in the faeces as microbiologically inactive compounds.

THERAPEUTIC INDICATIONS :
ZEFONE (Ceftriaxone) is indicated in the following clinical infections caused by microorganisms susceptible to Ceftriaxone :

- Lower respiratory tract infections such as bronchitis, pneumonia, bronchopneumonia, empyema, lung abscess etc.
- Acute bacterial otitis media.
- Skin and soft tissue infections such as abscesses, cellulitis, pyodermas, wound infections etc.
- Urinary tract infections (complicated and uncomplicated) such as urethritis, cystitis, pyelitis, pyelonephritis, perinephric abscess etc.
- Uncomplicated gonorrhoea
- Pelvic inflammatory disease
- Bacterial septicemia
- Intraabdominal infections
- Meningitis caused by susceptible organisms
- Prophylaxis - a single dose of Ceftriaxone injection administered pre-operatively may reduce chance of post- operative surgical infections.

DOSAGE AND ADMINISTRATION :
Zefone injection may be administered by deep intramuscular injection, slow intravenous injection, or as a slow intravenous infusion after reconstitution.

Adults and children 12 years and over :
Standard therapeutic dosage : 1 gm once daily.
Severe infections : 2-4 gm daily, normally as a single dose every 24 hours. The duration of therapy varies according to the course of the disease. As with other antibiotic therapy in general, administration of Zefone should be continued for a minimum of 48 to 72 hours after the patient has become a febrile or evidence of bacterial eradication has been obtained.

Acute uncomplicated gonorrhoea : a single dos of 250 mg intramuscularly should be administered.
Peri-operative prophylaxis : usually 1 gm as single intramuscular or slow intravenous dose. In colorectal surgery, 2 gm should be given intramuscularly or by slow intravenous injection or slow intravenous infusion, in conjunction with a suitable agent against anaerobic bacteria.

Use in elderly : These dosage do not require modification in elderly patients provided that renal and hepatic function are satisfactory.

Children under 12 years : Standard therapeutic dosage : 20-50 mg/kg body weight once daily. In severe infections up to 80 mg/kg body weight daily may be given. Doses of 50 mg/kg or over should be given by slow intravenous infusion over at least 30 minutes.

Renal and hepatic impairment : In patients with impaired renal function, there is no need to reduce the dosage of Zefone provided liver function is intact. Only in cases of pre-terminal renal failure (creatinine clearance < 10ml per minute) should the daily dosage be limited to 2 gm or less.

REVERSE

Preparation of solutions for injection and infusion : The use of freshly prepared solution is recommended. **Intramuscular injection** : 250 mg Zefone should be dissolved in 2 ml of 1% Lignocaine Hydrochloride injection, or 1 gm in 3.5 ml of 1% Lignocaine hydrochloride injection. The solution should be administered by deep intramuscular injection. Dosages greater than 1 gm should be divided and injected at more than one site. Solutions in lignocaine should not be administered intravenously.

Intravenous injection :250 mg of Zefone should be dissolved in 5 ml of water for injection or 1 gm in 10 ml of water for injections. The injection should be administered over 2-4 minutes, directly into the vein or via the tubing of an intravenous infusion.

Intravenous infusion : 2 gm of Zefone should be dissolved in 40 ml of one of the following calcium free solutions : Dextrose injection 5% or 10%, Sodium chloride injection, Sodium chloride and Dextrose injection (0.45% Sodium chloride and 2.5% dextrose). The infusion should be administered over at least 30 minutes. Solutions containing Zefone should not be mixed with or added to solutions containing other agents. In particular, Zefone is not compatible with calcium-containing solutions such as Hartmann's solution and Ringer's solution.

Reconstituted solutions are stable for 6 hours at room temperature and for 24 hours at 5°C.

CONTRAINDICATIONS :
ZEFONE is contraindicated in patients with known allergy to cephalosporin group of antibiotics. Zefone is also contraindicated in premature infants and in full-term infants during the first 6 weeks of life.

UNDESIRABLE EFFECTS :
ZEFONE has been generally well tolerated, with adverse reactions being relatively infrequent, usually mild and transient. The most common side effects are gastro-intestinal, consisting mainly of loose stools and diarrhoea or, occasionally, nausea, vomiting, stomatitis and glossitis. Cutaneous reactions, including maculopapular rash, pruritus, urticaria, oedema and erythema multiforme have occurred. Hematological reactions have included anaemia (all grades), leucopenia, neutropenia, thrombocytopenia, eosinophilia, agranulocytosis and positive Coomb's test. Regular blood counts should be carried out during treatment.

Zefone has rarely been associated with prolongation of prothrombin time. Headache and dizziness, drug fever, and transient elevations in liver function tests have been reported in a- few cases. Other rarely observed adverse reactions include glycosuria, oliguria, haematuria, anaphylaxis and bronchospasm. Pain or discomfort may be experienced at the site of intramuscular injection immediately after administration but is usually well tolerated and transient. Local phlebitis has occurred rarely following intravenous administration but can be minimised by slow injection over 2-4 minutes.

SPECIAL WARNINGS AND SPECIAL PRECAUTIONS FOR USE
Care is required when administering Zefone to patients who have previously shown hypersensitivity (especially anaphylactic reaction) to penicillins or other non-cephalosporin beta-lactam antibiotics, as occasional instances of cross-allergenicity between cephalosporins and hese antibiotics have been recorded. Anaphylactic shock requires immediate counter measures such as intravenous adrenaline injection followed by corticosteroid therapy. In severe renal impairment accompanied by hepatic insufficiency, dosage reduction is required. Pseudomembranous colitis has been reported with the use of cephalosporin group of antibiotics, and other broad spectrum antimicrobial agents. Therefore it is important to consider its diagnosis in patients who develop diarrhoea in association with use of the antibiotic. Ordinarily dosage adjustment is not required in hepatic failure. But in patients of both hepatic failure and significant renal dysfunction **ZEFONE** dosage should not exceed 2gm/day without close monitoring. Prolonged use may cause overgrowth of non-susceptible organisms and may cause superinfections. Administer with caution to patients with a history of G.I. diseases especially colitis.

DRUG INTERACTIONS :
No impairment of renal function has been observed in man after simultaneous administration of Ceftriaxone and diuretics.

No interference with the action or increase in nephrotoxicity of aminoglycosides has been observed during simultaneous administration with Zefone. The Ceftriaxone molecule does not contain the N methylthio- tetrazole substituent which has been associated with a disulfiram like effect when alcohol is taken during therapy with certain cephalosporins.

USE IN PREGNANCY AND LACTATION :
Zefone has not been associated with adverse effects on foetal development in laboratory animals but its safety in human pregnancy has not been established. Therefore it should not be used in pregnancy unless absolutely indicated. Low concentration of Ceftriaxone are excreted in human milk. Caution should be exercised when Ceftriaxone is administered to a nursing woman.

OVERDOSAGE :
In the case of overdosage, drug concentrations would not be reduced by haemodialysis or peritoneal dialysis. There is no specific antidote. Treatment should be symptomatic.

PRESENTATION :
Vial pack

STORAGE :
STORE BELOW 25°C
PROTECT FROM LIGHT & MOISTURE

KEEP OUT OF REACH OF CHILDREN

Zydus
Cadila

Marketed by : **Cadila Healthcare Limited**
"Zydus Tower", Satellite Cross Road,
Ahmedabad 380 015, India

Manufactured by:
Inject Care Parenterals Pvt. Ltd.
Plot No. 130, Silvassa Road,
G.I.D.C., Vapi - 396195. INDIA

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