negative bacteria including Pseudomonas aeruginosa. There have also been reports of enhanced activity in vitrowith other antibacterials including fosfomycin and ciprofloxacinand variable results with penicillins.Resistance may develop during treatment with cefotaximedue to derepression of chromosomally mediated betalactamases,and has been reported particularly inEnterobacter spp., with multiresistant strains emergingduring treatment. This type of resistance has also developedin other bacteria including Citrobacter, Serratia, andPseudomonas spp. Another mechanism of cefotaximeresistance is the development of plasma-mediated,extended-spectrum beta-lactamases, and this has occurredin Klebsiella spp. and also other Enterobacteriaceae. Resistance in Str. pneumoniae is due to the production of I altered penicillin-binding proteins.References to the antimicrobial activity of cefotaximeand other third-generation cephalosporins, including theproblem of bacterial resistance.

Dosage and Administration

Cefotaxime is a third-generation parenteral cephalospotinantibacterial used in the treatment of infections due to susceptible Gram-positive and Gram-negative bacteria, including infections of the abdomen, bones and joints, CNS, skin and skin structure, genito-urinary tract (including gonorrhoea) and respiratory· tract, in gynaecological infections, and in early Lyme disease. It is also used for surgical infection prophylaxis. For details of these infections All cross-references refer to entries in Volume Aand their treatment, see under Choice of Antibacterial, Cefotaxime is given as the sodium salt by deep intramuscniar injection or intravenously by slow injection over 3 to 5 minutes or by infusion over 20 to 60 minutes.

For mild to moderate infections cefotaxime is usually given in doses of 1 g 12 -hourly and increased to 1 to 2 g every 8 hours for moderate to severe infections. For septicaemia up to 6 to 8 g daily may be given in 3 to 4 divided doses, while in the most severe infections up to 12 g may be given daily by the intravenous route in up to 6 divided doses. Pseudomonal infections usually require more than 6 g daily, but a cephalosporin with greaterantipseudomonal activity, such as ceftazidime, is preferable. In the treatment of gonorrhoea, a single dose of 0.5 g or 1 g of cefotaxime is given. For surgical infection prophylaxis, 1 g is given 30 to 90 minutes before surgery. At caesarean section, 1 g is given intravenously to the mother as soon as the umbilical cord is clamped and two further doses intramuscularly or intravenously 6 and 12 hours later. The dose of cefotaxime may need to be reduced in patients with renal impairment. For details of doses in children, Cefotaxime may be used with an aminoglycoside a s synergy may occur against some Gram-negative organisms, but the drugs should be given separately. It has sometimes been used with another beta lactam to broaden the spectrum of activity. Cefotaxime has also been used with metronidazole in the treatment of mixed aerobic-anaerobic infections.

Intravenous injection

1. Reconstitute each 500-mg vial with 2mL WFI (use 4mL for each 1-g vial; 10mL for each 2-g vial) and shake well.
2. Withdraw the required dose.
3. The solution should be clear and straw-coloured. Inspect visually for particulate matter or discoloration prior to administration and discard if present.
4. Given by IV injection over 3-5 minutes.

Intermittent intravenous infusion

1. Reconstitute each 500-mg vial with 2mL WFI (use 4mL for each 1-g vial; 10mL for each 2-g vial) and shake well.
2. Withdraw the required dose and add to a suitable volume of compatible infusion fluid (usually 100mL NaCl 0.9%).
3. The solution should be clear and straw-coloured. Inspect visually for particulate matter or discoloration prior to administration and discard if present.
4. Given by IV infusion over 20-60 minutes.

Intramuscular injection

1. Reconstitute each 500-mg vial with 2mL WFI (use 4mL for each 1-g vial; 10mL for each 2-g vial) and shake well.
2. Withdraw the required dose.
3. Give by deep IM injection into a large muscle mass. Doses of 2 g should be distributed between two injection sites. Rotate injection sites for subsequent injections.

Adverse effects and Precautions

As for Cefalotin Sodium, Arrhythmias have been associated with rapid bolus dosage through a central venous catheter in a few cases. The broad-spectrum third-generation cephalospotinshave the potential for promoting colonisation and superinfectionwith resistant organisms such as Pseudomonas aeruginosa, Enterobacter spp., Candida, and enterococci, at various sites in the body, although the incidence has generally been low with cefotaxime. Changes in bowel flora are a predisposing factor and have been more marked with cefoperazone and ceftriaxone, possibly because of their greater biliary excretion. Pseudomembranous colitis, associated with Clostridium dijjidleinfection, may occasionally be seen with any of the third-generation cephalosporins. Reviews on adverse effects associated with third generation cephalospotins.

SIDE EFFECT

Frequent: Discomfort with IM administration, oral candidiasis (thrush), mild diarrhea, mild abdominal cramping, vaginal candidiasis.

Occasional: Nausea, serum sickness-like reaction (fever, join pain; usually occurs after second course of therapy and resolves after drug is discontinued).

Rare: Allergic reaction (rash, pruritus, urticaria), thrombophlebitis (pain, redness, swelling at injection site).

PREGNANCY

Pregnancy/Lactation: Readily crosses placenta. Distributed in breast milk.

PregnancyCategory B. Children: No agerelatedprecautions noted.

Elderly: Age-related renal impairment may require dosage adjustment.

OVERDOSAGE

Symptoms to watch for: Large doses have been associated with seizures.
Antidote: There is no known antidote but haemodialysis may be effective.
Stop administration and give supportive therapy as appropriate.

Storage: -Store Below 25° C, Protect from Light and moisture.
Improper Storage may deteriorate the product
Medicine: - Keep out of reach of children.
Presentation: -Each pack contain
A 1.0 gm. Vial of Cefotaxime Injection IP and sterile water for injection IP

Manufactured by:

AMERICAN REMEDIES
Care & Cure with Research
American Remedies Healthcare Pvt. Ltd.
(An ISO 9001-2015 Certified Company)

Gala No. 105 to 111, 1st Flr., Bldg. No. E-15/A, Hanhar Complex, Bhiwandi, Mumbai - 421302
At: Vill. Surajpur Nahan Road Paonta Sahib, Distt. Sirmour, Himachal Pradesh-173001
E-mail: info@americanremedies.in

WHO GMP CERTIFIED

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

℞ Cefotaxime Injection I.P.

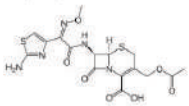
FOXATIM 1G
Injection

For IV/IM use only
Composition:-
Each Vial Contains:-
Cefotaxime Sodium (Sterile) IP
Eq. to anhydrous Cefotaxime 1000 mg.

Description

Cefotaxime sodium is a semisynthetic, broad spectrum cephalosporin antibiotic for parenteral administration. It is the sodium salt of 7-[2-(2-amino-4-thiazolyl) glyoxylamido]-3 (hydroxymethyl)-8-oxo-5-thia-1-azabicyclo [4.2.0] oct-2-ene-2-carboxylate 72 (Z)-(o-methyloxime), acetate (ester). The structural formula of Cefotaxime sodium is.

Cefotaxime sodium



CLINICAL PHARMACOLOGY

Following IM administration of a single 500 mg or 1 g dose of Cefotaxime Sodiumto normal volunteers, mean peak serum concentrations of 11.7 and 20.5 mcg/mL respectively were attained within 30 minutes and declined with an elimination half-life of approximately 1 hour. There was a dose-dependent increase in serum levels after the IV administration of 500 mg, 1 g, and 2 g of Cefotaxime Sodium (38.9, 101.7, and 214.4 mcg/mL respectively) without alteration in the elimination half-life. There is no evidence of accumulation following repetitive IV infusion of 1 g doses every 6 hours for 14 days as there are no alterations of serum or renal clearance. About 60% of the administered dose was recovered from urine during the first 6 hours following the start of the infusion.

Approximately 20-36% of an intravenously administered dose of 14C-cefotaxime is excreted by the kidney as unchanged cefotaxime and 15-25% as the desacetyl derivative, the major metabolite. Thedesacetyl metabolite has been shown to contribute to the bactericidal activity. Two other urinary metabolites (M2 and M3) account for about 20-25%. They lack bactericidal activity.

A single 50 mg/kg dose of Cefotaxime Sodium was administered as an intravenous infusion over a 10- to 15 minute period to 29 newborn infants grouped according to birth weight and age. The mean half-life of cefotaxime in infants with lower birth weights (≤1500 grams), regardless of age, was longer (4.6 hours) than the mean half-life (3.4 hours) in infants whose birth weight was greater than 1500 grams. Mean serum clearance was also smaller in the lower birth weight infants. Although the differences in mean halflife values are statistically significant for weight, they are not clinically important. Therefore, dosage should be based solely on age.

PHARMACOLOGY

Pharmacokinetics

Cefotaxime is given by injection as the sodium salt. It is rapidly absorbed after intramuscular injection and mean peak plasma concentrations of about 12 and 20 micrograms/ mL have occurred 30 minutes after doses of 500 mg and 1 g of cefotaxime, respectively. Immediately after intravenous injection of 0.5, 1, or 2 g of cefotaxime, meanpeak plasma concentrations of 38, 102, and 215 micrograms/ mL, respectively, has occurred with concentrations ranging from about 1 to 3 micrograms/mL after 4 hours. The plasma half-life of cefotaxime is about 1hour and that of the active metabolite desacetylcefotaxime about 1 . 5 hours; halflivesare increased in neonates and in patients with severe renal impairment, especially those of the metabolite, and a reduction in dosage may be necessary. The effects of liver disease on clearance of cefotaxime and its metabolite have been variable, but in general dosage adjustment has not been considered necessary. About 40% of cefotaxime is reported to be bound to plasma proteins. Cefotaxime and desacetylcefotaxime are widely distributed in body tissues and fluids; therapeutic concentrations occur in the CSF particularly when the meninges are inflamed. Cefotaxime crosses the placenta and low concentrations have been detected in breast milk. After partial metabolism in the liver to desacetylcefotaximeand inactive metabolites, elimination is mainly by the kidneys and about 40 to 60% of a dose has been recovered I unchanged in the urine within 24 hours; a further 20% is 1 excreted as the desacetyl metabolite. Relatively high concentrations of cefotaxime and desacetylcefotaxime occur in bile and about 2 0 % of a dose has been recovered in the faeces.

Probenecid competes for renal tubular secretion with cefotaxime resulting in higher and prolonged plasma concentrations of cefotaxime and its desacetyl metabolite. Cefotaxime and its metabolites are removed by haemodialysis. When microbiological assays have been used, reported pharmacokinetic values may relate to cefotaxime plus its active metabolite, desacetylcefotaxime.

Metabolism and Action

Cefotaxime is a third-generation cephalosporin. It has a bacteriddal action similar to cefamandole, but a broader spectrum of activity. It is highly stable to hydrolysis by most beta-lactamases and has greater activity than first- or second-generation cephalosporins against Gram-negative bacteria. Although cefotaxime is generally considered to have slightly less activity than first-generation cephalosporinsagainst Gram-positive bacteria, many streptococci are very sensitive.

Desacetylcefotaxime is an active metabolite of cefotaxime and there may be additive or synergistic effects against some species.

- Spectrum of activity. Among Gram-negative bacteria, cefotaxime is active in vitro against many Enterobacteriaceae including Citrobacter and Enterobacter spp., Escherichia coli, Klebsiella spp., both indole-positive and indole-negative Proteus, Providencia, Salmonella, Serratia, Shigella, and Yersinia spp. Other susceptible Gram-negative bacteria, including penicillin-resistant strains, are Haemophilusinfluenzae, Moraxella catarrhalis (Branhamellacatarrhalis), Neisseria gonorrhoeae, and N. meningitidis. Brucellamelitensis is also reported to be moderately sensitive. Some strains of Pseudomonas spp. are moderately susceptible to cefotaxime, but most are resistant. Desacetylcefotaxime is active against many of these, Gram-negative bacteria, but not against Pseudomonas spp.
- Among Gram-positive bacteria, cefotaxime is active against staphylococci and streptococci. Staphylococcus aureus, including penicillinase-producing strains but not meticillin-resistant Staph. aureus, is sensitive. Staph. epidermidis is also sensitive but penicillinase-producing strains are resistant. Streptococcus agalactiae (group B streptococci), Str. pneumoniae, and Str. pyogenes (group A streptococci) are all very sensitive although truly penicillin-resistant pneumococci are apparently not sensitive. Enterococci and Listeria monocytogenes are resistant.
- Cefotaxime is active against some anaerobic bacteria. Bacteroidesfragilis may be moderately sensitive, but many strains are resistant; synergy has been shown with desacetylcefotaxime in vitro. Clostridium perfringens is sensitive, but most Cl. difficile are resistant.
- Other organisms sensitive to cefotaxime include the spirochaeteBorreliaburgdorferi and Haemophilusducreyi. Activity with other antimicrobials. In addition to possible synergy or additive effects with desacetylcefotaxime, the activity of cefotaxime may be enhanced by aminoglycosides such as gentamicin; synergy has been shown in vitro against Gram-