CLAFOXIM

Vial

Composition
Each vial contains Cefotaxime (as sodium) equivalent to 1 gm Cefotaxime base.

Action
Clafoxim is a semi-synthetic cephalosporin antibiotic with a broad spectrum of activity against both Gram positive and Gram-negative bacteria. Clafoxim is bactericidal in its mode of action and has a high degree of stability in the presence of ß-lactamases.

Gram-positive aerobes
Staphylococcus aureus, including certain penicillinase and non-penicillinase producing strains, *Staphylococcus epidermidis*, Streptococcus Pyogenes (Group A ß-haemolytic streptococci), *Streptococcus agalactiae* (Group B streptococci) (Note: most strains of enterococci, e.g., S.faecalis are resistant), *Streptococcus pneumoniae*.

Gram-negative aerobes
Citrobacter species, Enterobacter species, *Escherichia coli, Haemophilus influenza* (including ampicillin-resistant H influenza), Klebsiella species (including K pneumoniae), *Neisseria gonorrhoeae, Proteus mirabilis, Morganella (Proteus) morganii, Proteus rettgeri, Proteus vulgaris*, Providencia species, Salmonella species, (including S. typhi), Serratia species, Shigella species. Cefotaxime and aminoglycosides have been shown to be synergistic in vitro against some strains of P. aeruginosa.

Anaerobes
Bacteroides species, Clostridium species (Note: most strains of C. difficile are resistant), Peptococcus species, Peptostreptococcus species.

Pharmacokinetics
Cefotaxime is administered by intramuscular and intravenous injection. After administration of a 1 gram dose, the mean plasma concentration is approximately 20 mg/l (intramuscular, t_{max} = 30 minutes), 102 mg/l (intravenous over 2-5 minutes), 27.9 mg/l (30 minute IV infusion). There is no significant evidence of accumulation after repetitive dosing in subjects with normal renal function. Mean elimination half life is 1.45 hour (IM), 1.06 hour (rapid IV) and 1.13 hour (30 minute IV infusion).

The desacetyl metabolite of Cefotaxime is detectable in blood and urine and is microbiologically active against a similar spectrum of bacteria, but is less active by a factor of 2 to 3. Approximately 20-36% of drug is excreted unchanged in the urine.

Cefotaxime is 32-44% bound to plasma protein and has a high renal clearance. 85-90% of the administered dose is recovered in the urine while the faeces accounted for 7-9.5% of the recovery total. 70-80% of the administered dose is recovered in the first 4 hours after administration.

The elimination half-life of Cefotaxime is 0.7-1.3 hours, whilst that of the metabolites is approximately 2 hours in patients with normal renal function. Mean peak urinary concentrations obtained after 1-gram administration of Cefotaxime, IM, IV, and IV infusion at 4 hours were 903 mg/l, 1309 mg/l and 599 mg/l, respectively.

Concentrations of Cefotaxime in the CSF are considerably lower than plasma.

Indications
Clafoxim is indicated for use primarily in the treatment of infections of the Genito urinary, gastrointestinal and respiratory tracts, in the skin and soft tissues and meningitis in children caused by susceptible strains of the following organisms:

- *Staphylococcal infections*: (including infections caused by both penicillinase-producing and non-penicillinase-producing strains): abscess, furunculosis, bronchitis and impetigo.

- *Streptococcal infections:* (both ß-haemolytic and group D streptococci), cellulitis, pneumonia, follicular tonsillitis, otitis media, pharyngitis, sinusitis, scarlet fever, septic sore throat, urinary tract infections (Enterococci) and meningitis in children.
- *Pneumococcal infections:* Lobar pneumonia, bronchitis, cellulitis and otitis media.
- *Haemophilus influenzae infections:* Otitis media, laryngotracheobronchitis and meningitis in children.
- *E coli infections*: Lobar pneumonia, urinary tract infections and meningitis in children.
- *Shigella infections:* Bacillary dysentery
- *Salmonella infections:* Enteritis
- *Sensitive strains of Pseudomonas aeruginosa:* Sepsis
- *Gonococcus:* Gonorrhoea
- *Neisseria Meningitidis:* Meningitis in children.

Bacteriological studies to determine the causative organisms and their sensitivity to Clafoxim should be performed.

Prophylactic uses
the administration of Clafoxim preoperatively may reduce the incidence of certain post-operative infections in patients undergoing surgical procedures that are classified as potentially contaminated. The minimum effective dose has been found to be 1 g Clafoxim 30-90 minutes prior to surgery.

Contraindications
Cefotaxime is contra-indicated in subjects allergic to cephalosporins.

Warnings
Cefotaxime must be used with caution in penicillin-sensitive subjects. Strict medical supervision is required throughout the treatment.

Adverse Reactions
Local Reactions
Deep phlebitis after IV injection has been reported.

General Reaction
Skin eruptions, fever, eosinophilia, neutropenia, transient leucopenia, and haemolytic anaemia. Granulocytopenia and agranulocytosis may develop during treatment with cefotaxime, particularly if given over long periods. For cases of treatment lasting longer than ten days, blood counts should therefore be monitored. Cases of diarrhoea have been recorded. The onset of diarrhoea may indicate the appearance of pseudomembranous colitis, the diagnosis of which should be confirmed by colonoscopy. This occurrence requires immediate cessation of administration and treatment with appropriate specific antibiotic therapy. Temporary elevation of transaminases and alkaline phosphatase has been recorded.

Interaction with Laboratory Tests
a false positive reaction can occur on testing for glucose in the urine with reducing substances, but this can be avoided with use of methods that are specific to gluco-oxidase.

Development of a positive Coombs'test may occur during treatment with cefotaxime.

Precautions
Stop the treatment should any allergic reaction appear.
Adapt the dosage in cases of organic or functional renal failure as mentioned under "Dosage and Administration".
Any combination with potentially nephrotoxic drugs and powerful diuretics should be taken into account in assessing the risks involved in such drug combinations

Pregnancy
Category B
Animal reproduction studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies in pregnant women.

Dosage and Administration

Intravenous and Intramuscular Injections
Dissolve Clafoxim in Water for Injection B P. Shake well until dissolved and then withdraw the entire contents of the vial into the syringe and use immediately.

Intravenous Infusion
Clafoxim may be administered by intravenous infusion using 1 g vials. 1 - 2 g are dissolved in 40 - 100 ml of Water for Injection B P or in the infusion fluids listed under “Stability in Infusion Fluids”.

The prepared infusion solutions should be administered over 20 - 60 minutes.

Dosage, route of administration and frequency of injections depend on the nature and severity of the infection, the condition of the patient, and the sensitivity of the pathogens to cefotaxime.

Adults
Usual dose 2 g daily, in 2 x 1 g injections. Severe cases may be given 3 - 4 g daily in 2 - 4 administrations. Very severe cases may be given up to 12 g I. V.

Neonates, Infants and Children
Neonates
The following dosage schedule is recommended :
0 - 1 week of age - 50 mg/kg I V q 12 h
1 - 4 weeks of age - 50 mg/kg I V q 8 h

It is not necessary to differentiate between premature and normal-gestational age infants.

Children and Infants
Usual daily dose 50 - 100 mg/kg body mass in 2 - 4 injections. In exceptional cases up to 200 mg/kg per day may be given.

Renal Failure
Because of extra-renal elimination, it is only necessary to reduce the dosage of Cefotaxime Sodium for Injection in severe renal failure (creatinine clearance <10 ml/min). After an initial loading dose of 1 g, the daily dose should be halved without change in the frequency of dosing, eg. 1 g 12 hourly becomes 0.5 g 12 hourly, 1 g 8 hourly becomes 0.5 g 8 hourly, and 2 g 8 hourly becomes 1 g 8 hourly.

Over Dosage

Treatment should be symptomatic and supportive.
In case of overdose, especially in renal impairment, there is a risk of reversible metabolic encephalopathy.

Presentation

Box of 1 gm vial