Cefotaxime pharmacology, Indications, Dosage, Adverse effects

Cefotaxime is an antibiotic of the cephalosporin group and has bactericidal effects. It's antibacterial activity against Gram-negative rod-shaped bacteria is many times stronger than that of the traditional cephalosporins and penicillins. In most pathogens, its minimum bacterialcidal concentration is slightly higher than its minimum inhibitory concentration.

In vitro studies of a combination of cefotaxime and aminoglycoside antibiotics reveals synergistic or additive effects. The serum protein binding is 32-50%, depending on the method used.

After injection, high cefotaxime clearly exceeding the susceptibility of most pathogens is obtained in serum, tissues, and body fluids.

Cefotaxime is primarily excreted through the kidneys in an antibacterially active form.

Pharmacokinetics

Following intramuscular administration of cefotaxime 500mg or 1g to normal volunteers, mean peak serum concentrations of 11.7 and 20.5 micrograms/mL respectively were obtained within 30 minutes and declined with an elimination half-life of approximately 1 hour.

There was a dose-dependent in increased serum levels after an intravenous administration of 500mg, 1g, and 2g of cefotaxime without alteration in the elimination half-life.

There is no evidence of accumulation following repetitive IV infusion of 1g of cefotaxime doses every 6 hours for 14 days as there are no alterations in serum or renal clearance.

About 60% of the administered dose was recovered from urine during the first six hours following the start of the infusion.

Approximately 20-36% of an intravenously administered dose 14c-Cefotaximeis excreted by the kidneys as unchanged cefotaxime and 15-25% as the desacetyl derivative, the major metabolite.

The desacetyl metabolite has been shown to contribute to bactericidal activity.

Two other urinary metabolites (M1 and M3) account for 20-25%. They lack bacteriocidal activity.

A single 50mg/kg of cefotaxime was administered as an intravenous infusion over 10-15 minutes to 29 newborn infants grouped according to birth weight and age. The mean half-life of cefotaxime in infants with lower birth weights (

Indications of cefotaxime

Cefotaxime is indicated for severe infections caused by cefotaxime-sensitive pathogens:

Infections of the:

1. Respiratory tract
2. Ear, nose and throat
3. Kidneys and urinary tract
4. Skin and soft tissues
5. Bones and joints
6. Genital organs, including gonorrhea
7. Abdominal region

Sepsis, endocarditis meningitis, preoperative prophylaxis in patients who are at an increased risk from infection, and for the prophylaxis of infections in patients with reduced resistance.

Cefotaxime is generally effective against the following microorganisms.

Staphylococci, aerobic and anaerobic streptococci, streptococcus pneumonia, Neisseria spp, Haemophilus influenzae, Escherichia coli, Citrobacter sppSalmonella spp, Enterobacter aerogenes, Serratia spp, indole positive and indole negative, Proteus spp, Yersinia entrocolitica, Clostridium spp, and Bacteroides spp.

Pathogens with varying susceptibility are

Streptococcus faecalis,Enterobacter cloacae, Pseudomonas aeruginosa and Bacterioides fragilis. There is no yet sufficient clinical experience with Salmonella typhy and Paratyphi A and B infections.

Cefotaxime is not effective against Treponema pallidum and clostridium defficile.

Combination Therapy

Cefotaxime can be combined with other antibiotics in life-threatening infections. The combination of cefotaxime and aminoglycosides is indicated without awaiting the results of sensitivity tests. The two preparations must be administered separately.

Infections with Pseudomonas aeruginosa may require concomitant treatment with other antibiotics effective against Pseudomonas.

Contraindications of cefotaxime

Cefotaxime is contraindicated in patients who have hypersensitivity to penicillins

Special warnings and precautions

In patients hypersensitive to penicillins or other beta-lactam antibiotics the possibility of cross-sensitivity exists

Renal function must be closely monitored in patients concomitantly treated with aminoglycosides

For courses of treatment lasting longer than 10 days, the blood count should be monitored closely

and treatment with cefuroxime be stopped if evidence of neutropenia is present

Administration of antibiotics especially prolonged course may lead to the proliferation of resistant microorganisms. The patient's condition must be therefore closely checked regularly

Cefotaxime should not be used in pregnancy especially in the first trimester unless otherwise strictly indicated.

As cefotaxime is excreted in breast milk, either breastfeeding or treatment of the mother with cefotaxime should be discontinued.

Adverse effects of cefotaxime

Effects on the blood picture: Thrombocytopenia, eosinophilia, and leukopenia

Effects on the liver: A rise in serum liver enzymes (SGOT, SGPT, Gamma-GT, Alkaline phosphatase, LDH) and bilirubin

Effects on the kidney: A transient increase in serum creatine and urea and in rare cases, interstitial nephritis may occur.

Effects on the gastrointestinal tract: Nausea and vomiting, abdominal pain, diarrhea. The possibility of pseudomembranous colitis must be considered.

Local reactions: Inflammatory irritation and pain at the site of injection.

Other reactions: Allergic skin reactions eg urticaria, exanthema, and itching may occur.

Drug fever and severe allergic reactions (anaphylaxis, sometimes progressing to shock) may occur and require emergency treatment.

Interactions

Probenecid may increase the concentration of cefuroxime in serum and prolong its duration of action.

Preparation of parenteral solution

Reconstitute with water for injection B.P already provided with the pack. Shake well until dissolved.

Use the quantity of water as suggested below

Vial size	Volume of diluent
250 mg	2ml
500mg	2ml
1g	4ml

Dosage

Neonates, infants, and children up to 12 years

Dosage, mode, and frequency of administration depend on the severity of the infections, sensitivity of the pathogen, and the condition of the patient. Unless otherwise prescribed, infants and children up to 12 years of age are given a daily dose of 50 - 100mg/kg body weight divided into equal doses at intervals of 6-12 hours.

In individual cases, patients with life-threatening infections were treated with daily amounts of 150-200mg/kg body weight; these doses were all tolerated.

Since renal clearance is not yet fully developed in premature infants, a daily dose of 50mg.kg body weight should not be exceeded. For the preoperative prophylaxis of infections, one of the above single dose is administered 30-60 minutes before the start of surgery. Depending on the risk of infection, the same dose may be repeated.

Adults and children over 12 years of age

Unless otherwise prescribes, adults and children over 12 years of age are given one vial of cefotaxime 1g every 12 hours.

In severe infections, the daily dose may be raised to a maximum of 12 g. If the daily dose is 4g, it may be divided into two wqual doses, administered at the injections or infusions are reduced to 8 to 6 hours.

The following table will serve as a guide

Types of infection	Single dose	Dose interval	Daily dose
Typical infections in which a highly sensitive pathogen is known or suspected	1g	12 hours	2g
Infection in which several pathogens of high to medium sensitivity are known or suspected	1-2g	12 hours	2-4g
Unidentified infections that cannot be localized and life threatening conditions	2-3g	6-8 hours	6-12g

For the treatment of gornorrhoea, a single dose of cefotaxime is administered intramuscularly.

For the preoperative prophylaxis of infections, the administration of 1-2g cefotaxime 30-60 minutes before surgery is recommended. Depending on the risk associated, the same dose may be repeated.

Dosage in patients with impaired renal function: In patients with a creatinine clearance of <50ml/minute, the maintenance dose should be reduced to laf the normal dose. The initial dose

depends on the sensitivity of the pathogen and the severity of the infection.

Duration of treatment: The duration of treatment depends on the patient's response. It should be continoued for atleast three says after the body temperature has returned to normal.

For continous drip infusion: 2g cefotaxime is dissolved on 100ml of the usual infusion solutions eg normal saline, ringers lactate solution, 5% dextrose solution, sodium lactate solution and administered over 50-60 minutes.

Sodium bicarbonate solutions must not be mixed with cefotaxime.

Reconstitution: The solution should be used immediately after reconstruction. After reconstitution, cefotaxime can be stored upto 24 hours at a temperature of below 25 degrees celcius without undergoing any significant physical or chemical changes