Bosch For Medical Professional Only

CEFOTAX® Injection

(Cefotaxime)

Sterile powder for injection

سیفوٹیکس انجکشن

(سیفوٹیکزِم)

DESCRIPTION:
Sterile CEFOTAX (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) having molecular formula C16H16N5NaO7S2 and molecular weight 477.5. Solutions of CEFOTAX range from very pale yellow to light amber depending on the concentration and the diluent used.

COMPOSITION:
Each Cefotax 0.25g vial contains:
Cefotaxime ..... 250mg as Cefotaxime sodium U.S.P.
(Product Specs.: U.S.P.)

Each Cefotax 0.5g vial contains:
Cefotaxime ..... 500mg as Cefotaxime sodium U.S.P.
(Product Specs.: U.S.P.)

Each Cefotax 1g vial contains:
Cefotaxime ..... 1000mg as Cefotaxime sodium U.S.P.
(Product Specs.: U.S.P.)

CLINICAL PHARMACOLOGY:
Pharmacodynamic properties:
Pharmacotherapeutic group: Beta-lactam antibiotics, cephalosporins. ATC Code: J01D D01

Mechanism of action:
Cefotaxime exerts its action by binding to one or more of the penicillin-binding proteins (PBPs) which in turn inhibits the final transpeptidation step of peptidoglycan synthesis in bacterial cell walls, thereby inhibiting cell wall synthesis.

Microbiology:
Gram-positive bacteria:
Enterococcus spp.
Staphylococcus aureus
Staphylococcus epidermidis
Streptococcus pneumoniae
Streptococcus pyogenes
Streptococcus spp.
Viridans group streptococci

Gram-negative bacteria:
Acinetobacter spp.
Citrobacter spp.
Enterobacter spp.
Escherichia coli
Haemophilus influenzae
Haemophilus parainfluenzae
Klebsiella spp.
Klebsiella pneumoniae
Morganella morganii
Neisseria gonorrhoeae
Neisseria meningitidis
Proteus mirabilis
Proteus vulgaris
Providencia rettgeri
Providencia stuartii
Serratia marcescens

Anaerobic bacteria:
Bacteroides spp.,
Bacteroides fragilis
Clostridium spp.
Ftusobacterium spp.
Fusobacterium nucleatum
Peptococcus spp.
Peptostreptococcus spp.

Pharmacokinetic properties
Absorption
Cefotaxime is for parenteral application. Mean peak concentrations 5 minutes after intravenous administration are about 81-102 mg/l following a 1 g dose of cefotaxime and about 167-214 mg/l 8 minutes after a 2 g dose. Intramuscular injection produces mean peak plasma concentrations of 20 mg/l within 30 minutes following a 1 g dose.

Distribution
Protein binding for cefotaxime is approximately 25-40%. The apparent distribution volume for cefotaxime is 21-37 l after 1 g intravenous infusion over 30 minutes.

Metabolism:
Cefotaxime is partly metabolised in humans. Approximately 15-25% of a parenteral dose are metabolised to the O-desacetyl-cefotaxime metabolite, which also has antibiotic properties.

Elimination
The main route of excretion of cefotaxime and O-desacetyl-cefotaxime is through the kidneys. Only a small amount (2%) of cefotaxime is excreted in the bile. The total clearance of cefotaxime is 240-390 ml/min and the renal clearance is 130-150 ml/min. In patients with severely impaired renal function (creatinine clearance 3-10 ml/min) the serum half- life of cefotaxime can be increased to 2.5-3.6 hours.

THERAPEUTIC INDICATIONS:
Cefotaxime sodium is indicated for the treatment of the following severe infections when known or thought very likely to be due to organisms that are susceptible to cefotaxime.

- Infections of the lower respiratory tract
- Infections of the kidneys and urinary tract
- Infections of the skin and soft tissue
- Genital infections caused by gonococci, particularly when penicillin has failed or is unsuitable
- Intra-abdominal infections (including Peritonitis)
- Lyme-borreliosis (especially stages II and III)
- Acute Meningitis in case of gram-negative microorganisms in combination with another suitable antibiotic
- Sepsis in case of gram-negative microorganism in combination with another suitable antibiotic
- Endocarditis in case of gram-negative microorganism in combination with another suitable antibiotic
- Peri-operative prophylaxis in surgical procedures such as colorectal, gastrointestinal, prostatic, urogenital and gynaecological surgery in patients who have a definite risk of post-operative infections.

DOSAGE AND ADMINISTRATION:
Adults and children over 12 years:
In general receive 1 g Cefotaxime every 12 hours. In severe cases, the daily dose can be increased up to 12 g. Daily doses up to 6 g can be divided into at least two individual administrations at 12 hourly intervals. Higher daily doses must be divided into at least 3 to 4 individual administrations at 8 or 6 hour intervals respectively. For the treatment of gonorrhoea in adults, 1 vial of Cefotaxime Sodium for Injection 500mg administered as a single administration.

Perioperative Prophylaxis
The administration of a single dose of 1 to 2 g Cefotaxime 30 to 60 minutes prior to the operation is recommended. Another antibiotic to cover anaerobic organisms is necessary. A repeat dose is required if the duration of the operation exceeds 90 minutes.

Infants and children up to 12 years
Infants and children up to 12 years receive 50 to 100 mg Cefotaxime according to the severity of the infection (up to 150 mg) per kilogram of body weight per day, divided into equal doses, administered at 12 (up to 6) hour intervals. In individual cases, particularly in life threatening situations, it may be necessary to increase the daily dose to 200 mg Cefotaxime per kilogram of body weight.

In neonates and infants
In neonates and infants doses of 50 mg Cefotaxime per kilogram of body weight per day should not be exceeded in view of not fully matured kidney clearance. In case of life-threatening situations it may be necessary to increase the daily dose as follow:

Age	Daily Dose of Cefotaxime
0 – 7 days	50 mg/kg every 12 hours IV
7 days – 1 month	50 mg/kg every 8 hours IV
> 1 month	75 mg/kg every 8 hours IV

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

Elderly:
No dosage adjustment is required provided that renal and hepatic function are normal.

Patients with renal impairment:
With patients with a creatinine clearance of 20ml/minute or less, the maintenance dose is reduced to half the normal dose. With patients with a creatinine clearance of 5 ml/minute or less, a reduction of the maintenance dose to 1 g Cefotaxime (divided into 2 individual administrations at 12 hour intervals). Cefotaxime is to a large extent eliminated by haemodialysis, an additional dose should be administered to patients who are dialysed, after the dialysis procedure.

Method of administration:
Intravenous Injection
For IV, Cefotaxime Sodium for Injection 250mg and 500mg is dissolved in at least 2 ml water for injections, Cefotaxime Sodium for Injection 1 g in at least 4 ml and subsequently injected directly into the vein over 3 to 5 minutes or after clamping of the infusion tube into the distal end of the tube.

Infusion
For brief infusion 2g of Cefotaxime Sodium for Injection is dissolved in 100 ml of isotonic sodium chloride or glucose solution and subsequently IV infused over 50 to 60 minutes.

Intramuscular Injection
For intramuscular injection. Cefotaxime Sodium for Injection 250mg and 500mg is dissolved in 2 ml and Cefotaxime Sodium for Injection 1 g in 4 ml water for injections respectively. Afterwards the injection should take place deep into the gluteal muscle. Pain with the IM injection can be avoided by dissolving Cefotaxime Sodium for Injection 500mg in 2ml or Cefotaxime Sodium for Injection 1 g in 4 ml 1% lidocaine solution.
It is recommended that no more than 4 ml be injected unilaterally. If the daily dose exceeds 2 g Cefotaxime or if Cefotaxime is injected more frequently than twice per day, the IV route is recommended.

CONTRAINDICATIONS:
Cefotaxime is contraindicated in patients who have shown hypersensitivity to cefotaxime sodium, or the cephalosporin group of antibiotics.

WARNINGS AND PRECAUTIONS
Allergies or asthma
Hypersensitivity to penicillin and other β-lactam antibiotics is necessary before prescribing cephalosporins since cross allergy occurs in 5-10% of cases. Use of cephalosporins should be undertaken with extreme caution in penicillin-sensitive patients. . If a hypersensitivity reaction occurs, treatment must be stopped. The use of cefotaxime is strictly contraindicated in subjects with a history of immediate-type hypersensitivity to cephalosporins.

Serious bullous reactions
Serious bullous skin reactions such as Stevens-Johnson syndrome or toxic epidermal necrolysis have been reported with cefotaxime. Patients should be advised to contact their doctor immediately prior to continuing treatment if skin or mucosal reactions occur.

Clostridium difficile associated disease
CDAD may range in severity from mild to life threatening, the most severe form of which is pseudomembranous colitis.It is important to consider this diagnosis in patients who present with diarrhoea during or subsequent to the administration of cefotaxime. If a diagnosis of pseudomembranous colitis is suspected, cefotaxime should be stopped immediately and appropriate specific antibiotic therapy should be started without delay.

Haematological reactions
Leucopenia, neutropenia and more rarely, agranulocytosis, may develop during treatment with cefotaxime, particularly if given over long periods. For treatment courses lasting longer than 7-10 days, the blood white cell count should be monitored and treatment stopped in the event of neutropenia. Cases of haemolytic anaemia have also been reported.

Neurotoxicity
High doses of beta lactam antibiotics including cefotaxime, particularly in patients with renal insufficiency Patients should be advised to contact their doctor immediately prior to continuing treatment if such reactions occur.

Precautions for administration
Potentially life-threatening arrhythmia has been reported in a very few patients who received rapid intravenous administration of cefotaxime through a central venous catheter. The recommended time for injection or infusion should be followed.

Effects on Laboratory Tests
As with other cephalosporins, a positive Coombs test has been found in some patients treated with cefotaxime and can interfere with cross-matching of blood. Urinary glucose testing with non-specific reducing agents may yield false positive results.

Sodium intake
The sodium content of this product should be taken into account when prescribing to patients requiring sodium restriction.

DRUG INTERACTIONS
Other Antibiotics
Cefotaxime should not be combined with substances having a bacteriostatic action (e.g. tetracycline, erythromycin, chloramphenicol or sulfonamides), A synergistic effect can result with the combination with aminoglycosides. An increased risk of nephrotoxicity has been reported when cefotaxime has been used concomitantly with cephalosporins or aminoglycosides. Dose adjustment may be necessary, and the kidney function must be watched.

Probenecid
The simultaneous administration of Probenecid leads to higher, more prolonged plasma concentrations of Cefotaxime by interfering with renal tubular transfer thereby delaying excretion.
Potentially Nephrotoxic Drugs and Loop Diuretics
In combination with potentially nephrotoxic drugs and with potent diuretics, (e.g. furosemide) the kidney function should be monitored.

ADVERSE EFFECTS:
Very Common: Pain at the injection site

Uncommon: Leukopenia, eosinophilia, thrombocytopenia, jarischherxheimer reaction, convulsions, diarrhea, increase in liver enzymes or bilirubin, rash, pruritus, urticaria, decrease in renal function/ increase of creatinine, fever inflammatory reactions at the injection site, including phlebitis/ thrombophlebitis.

Not Known: Superinfection, neutropenia agranulocytosis, haemolytic anaemia, anaphylactic reactions, angioedema, bronchospasm, anaphylactic shock, headache, dizziness, encephalopathy, arrhythmia following rapid bolus infusion through central venous catheter, nausea, vomiting, abdominal pain, pseudomembranous colitis, hepatitis, erythema multiforme, stevens-johnson syndrome, toxic epidermal necrolysis, interstitial nephritis. for im formulations (since the solvent contains lidocaine): systemic reactions to lidocaine

USE IN PREGNANCY AND LACTATION:
Pregnancy:
The safety of cefotaxime has not been established in human pregnancy. Cefotaxime passes through the human placenta. Cefotaxime should only be used during pregnancy if the anticipated benefit outweighs any potential risks.

Lactation:
CEFOTAX is excreted in human milk in low concentrations. Caution should be exercised when CEFOTAX is administered to a nursing woman

OVERDOSE:
Symptoms of overdose may largely correspond to the profile of side effects. In case of overdose, cefotaxime must be discontinued and supportive treatment initiated. Drug initiated cramps can be treated with diazepam or phenobarbital, but not with phenytoin. With anaphylactic reactions the usual emergency measures must be commenced, preferably with the first indications. No specific antidote exists. Plasma levels of cefotaxime can be reduced by haemodialysis or peritoneal dialysis.

Special precautions for disposal and other handling
Following reconstitution Cefotaxime sodium is compatible with the following diluents:
Water for Injections
Sodium Chloride 0.9%
Dextrose 5 and 10%
Ringer's Solution
Ringer-Lactate Solution
Lignocaine 1% (only freshly prepared solutions should be used).

Shelf life
3 years
Following reconstitution: 24 hours

PRESENTATION
Cefotax 0.25gm Injection: Pack of 1 vial +1 ampoule of 2ml sterile water for injection as solvent.
Cefotax 0.5gm Injection: Pack of 1 vial +1 ampoule of 2ml sterile water for injection as solvent.
Cefotax 1gm Injection: Pack of 1 vial +1 ampoule of 5ml sterile water for injection as solvent.

Storage and Instructions:
- Protect from heat, sunlight & moisture, store below 30°C.
- The Expiration date refers to the product correctly stored at required condition.
- Keep out of the reach of children.
- Patients and healthcare professionals can also report suspected adverse drug reaction at ade@bosch-pharma.com.
- To be sold on prescription of a registered medical practitioner only.

بچوں/ وریدی استعمال کے لیے۔

ہدایات:-

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

دھوپ، گرمی اور نمی سے محفوظ ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔

بچوں کی پہنچ سے دُور رکھیں۔

صرف مستند ڈاکٹر کے نسخے پر فروخت کے لئے۔

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ISO 9001:2015 Certified Company