EXEF 250mg, 500mg & 1g Inj.

(Cefotaxime) Injection USP

Long acting, broad spectrum cephalosporin antibiotic for parenteral use.

1. EXEF Injection 250mg
One vial of Sterile Cefotaxime Sodium USP equivalent to Cefotaxime 250mg.
Product Specification: USP.

2. EXEF Injection 500mg
One vial of Sterile Cefotaxime Sodium USP equivalent to Cefotaxime 500mg.
Product Specification: USP.

3. EXEF Injection 1g
One vial of Sterile Cefotaxime Sodium USP equivalent to Cefotaxime 1g.
Product Specification: USP.

DESCRIPTION:
Sterile EXEF (Cefotaxime Sodium) is a semi synthetic, broad spectrum cephalosporin antibiotic for parenteral administration, EXEF is supplied as dry powder in vials, while each vial of 250mg EXEF contains 262.5mg of anhydrous Cefotaxime Sodium (Equivalent to 250mg Cefotaxime), each vial of 500mg EXEF contains 525mg of anhydrous Cefotaxime Sodium (Equivalent to 500mg Cefotaxime) and each vial of 1g EXEF contains 1.05g of anhydrous Cefotaxime Sodium (equivalent to 1g cefotaxime).

CLINICAL PHARMACOLOGY:
Following IM administration of a single 500mg or 1g dose of Cefotaxime, mean peak serum concentrations of 11.7 and 20.5mcg/ml respectively were attained within 30 minutes and declined with an elimination half-life of approximately 1 hour. There is no evidence of accumulation following repetitive IV infusion of 1g doses every six 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 infusion.

Cefotaxime is excreted by the kidney as unchanged Cefotaxime and 15 – 25% as the desacetyl derivative, the major metabolite. The desacetyl metabolite has been shown to contribute to the bactericidal activity. The mean half-life of Cefotaxime in infants with lower birth weight, i.e. lesser than or equal to 1500 grams, was (4.6 hours) than the mean half-life is (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 half-life values are statistically significant for weight, they are not clinically important. Therefore, dosage should be based solely on age.

MICROBIOLOGY:
The bactericidal activity of Cefotaxime Sodium results from inhibition of cell wall synthesis. Cefotaxime Sodium has in vitro activity against a wide range of gram-positive and gram-negative organisms. Cefotaxime Sodium has been shown to be a potent inhibitor of b-lactamases produced by certain gram-negative bacteria. Cefotaxime sodium is usually active against the following microorganisms both in vitro and in clinical infections.

AEROBES, GRAM-POSITIVE:
Staphylococcus aureus, including pencillinase and non- pencillinase producing strains, Staphylococcus epidermidis, Enterococcus species, Streptococcus pyogenes, Streptococcus agalactiae, Streptococcus pneumoniae (formerly Diplococcus pneumoniae).

AEROBES, GRAM-NEGATIVE:
Citrobacter species, Enterobacter species, Escherichia coli, Haemophilus influenzae (including ampicillin-resistant -H. influenzae), Haemophilus parainfluenzae, Klebsiella species, Neisseria gonorrhoeae, Neisseria meningitidis, Proteus mirabilis, Proteus vulgaris, Proteus inconstans Group B, Morganella morganii, Providencia rettgeri, Serratia species and Acinetobacter species.

Cefotaxime Sodium is active against some strains of pseudomonas aeruginosa.

ANAEROBES:
Bacteroides species, including some strains of B. fragilis, Clostridium species, Peptococcus species. The drug is also stable to b-lactamase (penicillinase) produced by staphylococci. In addition, Cefotaxime Sodium shows high affinity for penicillin-binding proteins in the cell wall. Cefotaxime Sodium and aminoglycosides have been shown to be synergistic in vitro against some strains of Pseudomonas aeruginosa.

SUSCEPTIBILITY TESTS:
Quantitative methods that require measurement of zone diameters give the most precise estimate of antibiotic susceptibility. Susceptible organisms produce zones of 20 mm or greater, indicating that the tested organism is likely to respond to therapy. Organisms that produce zones of 15 to 19 mm are expected to be susceptible if high dosage is used or if the infection is confined to tissues and fluids (e.g. urine) in which high antibiotic levels are attained. Resistant organisms produce zones of 14 mm or less, indicating that other therapy should be selected.
Organisms should be tested with the Cefotaxime Sodium disc a bacterial isolate may be considered susceptible if the MIC value for Cefotaxime Sodium is not more than 16mg/ml. Organisms are considered resistant to Cefotaxime Sodium if the MIC is equal to or greater than 64µg/ml.

INDICATIONS AND USAGE:
(I) Lower respiratory tract infections, including pneumonia, caused by Streptococcus pneumoniae, Streptococcus pyogenes and other streptococci, Staphylococcus aureus, Klebsiella species, Haemophilus influenzae, Haemophilus parainfluenzae, Proteus mirabilis and Serratia marcescens.

(II) Genitourinary infections, Urinary tract infections caused by Enterococcus species, Staphylococcus epidermidis, Staphylococcus aureus, Citrobacter species, Enterobacter species, Escherichia coli, Klebsiella species, Proteus mirabilis, Proteus vulgaris, proteus inconstans group B, Morganella morganii, Serratia marcescens, and Pseudomonas species.

(III) Gynecological infections, including pelvic inflammatory disease, endometritis and pelvic cellulitis caused by Staphylococcus epidermidis, Staphylococcus aureus, Streptococcus species, Enterococcus species, Klebsiella species, Escherichia coli, Proteus mirabilis, Bacteroides species and Clostridium species.

(IV) Bacteremia / Septicemia, caused by Escherichia coli, Klebsiella species, Serratia marcescens, Staphylococcus aureus, and Streptococcus species.

(V) Skin and skin structure infections, caused by Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus pyogenes and other streptococci, Enterococcus species, Acinetobacter species, Escherichia coli, Citrobacter species, Proteus mirabilis, Proteus vulgaris, Morganella morganii, Providencia rettgeri, Bacteroides species, and anaerobic cocci.

(VI) Intra-abdominal infections, including peritonitis caused by Streptococcus species, Escherichia coli, Klebsiella species, Bacteroides species and anaerobic cocci (including Peptostreptococcus species and Peptococcus species) Proteus mirabilis and Clostridium species.

(VII) Bone and / or joint infections, caused by Staphylococcus aureus (penicillinase and non-penicillinase producing strains), Streptococcus species (including S. pyogenes), Pseudomonas species (including P. aeruginosa), and Proteus mirabilis.

(VIII) Central nervous system infections e.g. meningitis and ventriculitis, caused by Neisseria meningitidis, Haemophilus influenzae, Streptococcus pneumoniae, Klebsiella pneumoniae, and Escherichia coli.

PREVENTION:
The administration of EXEF (Cefotaxime Sodium) preoperatively reduces the incidence of certain infections in patients undergoing surgical procedures (e.g. abdominal or vaginal hysterectomy, gastrointestinal and genitourinary tract surgery) that may be classified as contaminated or potentially contaminated. In patients undergoing cesarean section, intraoperative and postoperative use of EXEF (Cefotaxime Sodium) may also reduce the incidence of certain postoperative infections.

CONTRAINDICATIONS:
EXEF (Cefotaxime Sodium) is contraindicated in patients who have shown hypersensitivity to the cephalosporin group of antibiotics.

DOSAGE AND ADMINISTRATION:
Adults: Dosage and route of administration should be determined by susceptibility of the causative organisms, severity of the infection, and the condition of the patient (see table for dosage guidelines).

Guidelines for Dosage of EXEF:

Types of Infection	Daily Dose (grams)	Frequency of Route
Gonococcal urethritis /cervicitis in males and females	0.5	0.5 gram IM (single dose)
Rectal gonorrhoea in females	0.5	0.5 gram IM (single dose)
Rectal gonorrhoea in males	1	1 gram IM (single dose)
Uncomplicated infections	2	1 gram every 12 hours IM or IV
Moderate to severe infections	3-6	1-2 grams every 8 hours IM or IV
Infections commonly needing antibiotics in higher dosage (e.g. septicemia)	6-8	2 grams every 6-8 hours IV
Life-threatening infections	up to 12	2 grams every 4 hours IV

EXEF may be administered IM or IV after reconstitution. Premixed EXEF Injection intended for IV administration after thawing. The maximum daily dosage should not exceed 12 grams.

Cesarean section patients:
The first dose of 1gram is administered intravenously as soon as the umbilical cord is clamped. The second and third doses should be given as 1gram intravenously or intramuscularly at 6 and 12 hours after the first dose.

Neonates, Infants and Children:
The following dosage schedule is recommended:

Neonates (birth to 1 month):
0-1 week of age 50mg/kg per dose every 12 hours IV.
1-4 weeks of age 50mg/kg per dose every 8 hours IV.
It is not necessary to differentiate between premature and normal-gestational age infants.

Infants and Children (1 month to 12 years):
For body weight less than 50kg, the recommended daily dose is 50 to 180mg/kg IM or IV body weight divided into four to six equal doses. The higher dosages should be used for more severe or serious infections, including meningitis. For body weight 50kg or more, the usual adult dosage should be used; the maximum daily dosage should not exceed 12 grams.

IM ADMINISTRATION:
As with all IM preparations, EXEF (Cefotaxime Sodium) should be injected well within the body of a relatively large muscle such as the upper outer quadrant of the buttock (i.e., gluteus maximus); aspiration is necessary to avoid inadvertent in jection into a blood vessel. Individual IM doses of 2 grams may be given if the dose is divided and is administered in different intramuscular sites.

IV ADMINISTRATION:
The IV route is preferable for patients with bacteremia, bacterial septicemia, peritonitis, meningitis or other severe or life-threatening infections, or for patients who may be poor risks because of lowered resistance resulting from such debilitating, conditions as malnutrition, trauma, surgery, diabetes, heart failure, or malignancy, particularly if shock is present or impending.

For intermittent IV administration, a solution containing 1gram or 2 grams in 10ml of Sterile Water for Injection can be injected over a period of three to five minutes. Cefotaxime should not be administered over a period of less than three minutes. With an infusion system, it may also be given over a longer period of time through the tubing system by which patient may be receiving other IV solution. However, during infusion of the solution containing EXEF (Cefotaxime Sodium). It is advisable to discontinue temporarily the administration of other solutions at the same site.

WARNINGS AND PRECAUTIONS:
BEFORE THERAPY WITH EXEF (CEFOTAXIME SODIUM) IS INSTITUTED CAREFUL INQUIRY SHOULD BE MADE TO DETERMINE WHETHER THE PATIENT HAS HAD PREVIOUS HYPERSENSITIVITY REACTIONS TO CEFOTAXIME SODIUM, CEPHALOSPORINS, PENICILLINS OR OTHER DRUGS.

• SCARS including acute generalized exanthematous pustulosis (AGEP), Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and DRESS, which can be life-threatening or fatal, have been reported post- marketing in association with cefotaxime/ethambutol treatment.

• At the time of prescription patients should be advised of the signs and symptoms for skin reactions.

• If signs and symptoms suggestive of these reactions appear, cefotaxime/ethambutol should be withdrawn immediately.

• If the patient has developed AGEP, SJS, TEN or DRESS with the use of cefotaxime / ethambutol, treatment with cefotaxime / ethambutol must not be restarted and should be permanently discontinued.

• In children, the presentation of a rash can be mistaken for the underlying infection or an alternative infectious process, and physicians should consider the possibility of a reaction to cefotaxime/ethambutol in children who develop symptoms of rash and fever during therapy with cefotaxime/ethambutol.

EXEF (Cefotaxime Sodium) should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.
Because high and prolonged serum antibiotic concentrations can occur from usual dose in patients with transient or persistent reduction of urinary output because of renal insufficiency, the total daily dosage should be reduced when EXEF is administered to such patients. Continued dosage should be determined by degree of renal impairment, severity of infection and susceptibility of the causative organism.
Although there is no clinical evidence supporting the necessity of changing the dosage of Cefotaxime Sodium in patients with even profound renal dysfunction. It is suggested that until further data is obtained the dose of Cefotaxime Sodium be halved in patients with estimated creatinine clearance of less than 20ml/min/1.73 m^2.
When only serum creatinine is available, the following formula (based on sex, weight and age of the patient) may be used to convert this value into creatinine clearance. The serum creatinine should represent a steady state of renal function.

Males: $\frac{\text{weight (kg) x (140-age)}}{\text{72 x serum creatinine}}$

Females: 0.85 x above value

ADVERSE REACTIONS:
EXEF (Cefotaxime Sodium) is generally well tolerated. The most common adverse reactions have been local reactions following IM or IV injection. Other adverse reactions have been encountered infrequently.

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) with frequency "Not known".

STORAGE:
Store below 30°C in dry form.
Protect from heat, light and moisture.

HOW TO SUPPLIED:
I) EXEF 1g vial with a 5ml ampoule of sterile water for injection.
II) EXEF 500mg vial with a 5ml ampoule of sterile water for injection.
III) EXEF 250mg vial with a 5ml ampoule of sterile water for injection.

Keep all medicines out of the reach of children.

Manufactured by :
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