Clafort
(Cefotaxime Sodium)

IM / IV INJECTIONS

کلے فورٹ
(سیفوٹیکسیم سوڈیم)

آئی ایم/ آئی وی انجکشن

COMPOSITION:

Clafort Injection 250mg IM/IV:
Vial: Cefotaxime Sodium U.S.P. equivalent to Cefotaxime 250mg
Ampoule: Water for Injection B.P. ..... 5 ml

Clafort Injection 500mg IM/IV:
Vial: Cefotaxime Sodium U.S.P. equivalent to Cefotaxime 500mg
Ampoule: Water for Injection B.P. ..... 10 ml

Clafort Injection 1g IM/IV:
Vial: Cefotaxime Sodium U.S.P. equivalent to Cefotaxime 1g
Ampoule: Water for Injection B.P. ..... 10 ml

Clafort Injection 2g IV:
Vial: Cefotaxime Sodium U.S.P. equivalent to Cefotaxime 2g
Ampoule: Water for Injection B.P. ..... 10 ml

DESCRIPTION:

Clafort contains cefotaxime, belongs to the class of drugs called third generation cephalosporins, off white to pale yellow crystalline powder. It is soluble in water at about 20%, but poorly soluble in common organic solvents including ethanol. It is available in injectable form for IV and IM administration.

PHARMACOLOGY:

Mechanism of action

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

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 a high degree of stability in the presence of ß-lactamases, both penicillinases and cephalosporinases, of gram-negative and gram-positive bacteria. Cefotaxime sodium has been shown to be active against most strains of the following microorganisms both in vitro and in clinical infections as described in the indication and usage section.

Aerobes, Gram-Positive

Enterococcus spp.
Staphylococcus aureus*, including ß-lactamase-positive and negative strains
Staphylococcus epidermidis
Streptococcus pneumoniae
Streptococcus pyogenes (Group A beta-hemolytic streptococci)
Streptococcus spp.
*Staphylococci which are resistant to methicillin / oxacillin must be considered resistant to cefotaxime sodium

Aerobes, Gram-Negative

Acinetobacter spp.
Citrobacter spp.
Enterobacter spp.
Escherichia coli
Haemophilus influenzae (Including ampicillin-resistant strains)
Haemophilus parainfluenzae
Klebsiella spp. (Including Klebsiella pneumoniae)
Morganella morganii
Neisseria gonorrhoeae (Including ß-lactamase-positive and negative strains)
Neisseria meningitidis
Proteus mirabilis
Proteus vulgaris
Providencia rettgeri
Providencia stuartii
Serratia marcescens

NOTE: Many strains of the above organisms that are multiply resistant to other antibiotics, e.g. penicillins, cephalosporins, and aminoglycosides, are susceptible to cefotaxime sodium. Cefotaxime sodium is active against some strains of Pseudomonas aeruginosa.

Anaerobes:

Bacteroides spp., including some strains of Bacteroides fragilis
Clostridium spp. (Note: Most strains of Clostridium difficile are resistant)
Fusobacterium ssp. (Including Fusobacterium nucleatum)
Peptococcus spp.
Peptostreptococcus spp.

Aerobes, Gram-negative

Providencia spp.
Salmonella spp. (Including Salmonella typhi)
Shigella spp.

Cefotaxime sodium and aminoglycosides have been shown to be synergistic in vitro against some strains of Pseudomonas aeruginosa but the clinical significance is unknown.

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 micro-grams/mL have occurred 30 minutes after doses of 500 mg and 1 g of cefotaxime, respectively. Immediately after intravenous injection of 500 mg, 1, or 2 g of cefotaxime, mean peak plasma concentrations of 38, 102, and 215 micro-grams/mL, respectively, have occurred with concentrations ranging from about 1 to 3 micrograms/mL after 4 hours. The plasma half-life of cefotaxime is about 1 hour and that of the active metabolite desacetylcefotaxime about 1.5 hours; half-lives are 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 desacetylcefotaxime and inactive metabolites. elimination is mainly by the kidneys and about 40 to 60% of a dose has been recovered unchanged in the urine within 24 hours; a further 20% is excreted as the desacetyl metabolite. Relatively high concentrations of cefotaxime and desacetylcefotaxime occur in bile and about 20% 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 hemodialysis. When microbiological assays have been used, reported pharmacokinetic values may relate to cefotaxime plus its active metabolite, desacetylcefotaxime.

INDICATIONS AND USAGE :

Clafort is indicated for the treatment of patients with serious infections caused by susceptible strains of the designated microorganisms in the diseases listed below.

- **Lower respiratory tract infections.** Including pneumonia, caused by Streptococcus pneumoniae (formerly Diplococcus pneumoniae), Streptococcus pyogenes (Group A streptococci) and other streptococci (excluding enterococci, e.g., Enterococcus faecalis), Staphylococcus aureus (penicillinase and non-penicillinase producing), Escherichia coli, Klebsiella species, Haemophilus influenzae (including ampicillin resistant strains), Haemophilus parainfluenzae, Proteus mirabilis, Serratia marcescens, Enterobacter species, indole positive Proteus and Pseudomonas species (including P. aeruginosa).
- **Genitourinary infections.** Urinary tract infections caused by Enterococcus species, Staphylococcus epidermidis, Staphylococcus aureus, (penicillinase and non-penicillinase producing), Citrobacter species, Enterobacter species, Escherichia coli, Klebsiella species, Proteus mirabilis, Proteus vulgaris, Providencia stuartii, Morganella morganii, Providencia rettgeri, Serratia marcescens and Pseudomonas species (including P. aeruginosa). Also, uncomplicated gonorrhea (cervical/urethral and rectal) caused by Neisseria gonorrhoeae, including penicillinase producing strains.
- **Gynecologic infections.** Including pelvic inflammatory disease, endometritis and pelvic cellulitis caused by Staphylococcus epidermidis, Streptococcus species, Enterococcus species, Enterobacter species, Klebsiella species, Escherichia coli, Proteus mirabilis, Bacteroides species (including Bacteroides fragilis), Clostridium species, and anaerobic cocci (including Peptostreptococcus species and Peptococcus species) and Fusobacterium species (including F. nucleatum).
- **Bacteremia/Septicemia.** Caused by Escherichia coli, Klebsiella species, and Serratia marcescens, Staphylococcus aureus and Streptococcus species (including S. pneumonia).
- **Skin and skin structure infections.** Caused by Staphylococcus aureus (penicillinase and non-penicillinase producing), Staphylococcus epidermidis, Streptococcus pyogenes (Group A streptococci) and other streptococci, Enterococcus species, Acinetobacter species, Escherichia coli, Citrobacter species (including C. freundii), Enterobacter species, Klebsiella species, Proteus mirabilis, Proteus vulgaris, Morganella morganii, Providencia rettgeri, Pseudomonas species, Serratia marcescens, Bacteroides species, and anaerobic cocci (including Peptostreptococcus species and Peptococcus species).
- **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.
- **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.
- **Central nervous system infections.** e.g., meningitis and ventriculitis, caused by Neisseria meningitidis, Haemophilus influenzae, Streptococcus pneumoniae, Klebsiella pneumoniae and Escherichia coli.
- **Prophylaxis.** The administration of Clafort 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.

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. Clafort may be administered IM or IV after reconstitution. The maximum daily dosage should not exceed 12 grams. The following guidelines is used for infections.

Type of Infection	Daily Dose (grams)	Frequency and Route
Gonococcal urethritis/ cervicitis in males and females	0.5	0.5gram IM (single dose)
Rectal gonorrhea in females	0.5	0.5gram IM (single dose)
Rectal gonorrhea 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

If C. trachomatis is a suspected pathogen, appropriate anti-chlamydial coverage should be added, because cefotaxime sodium has no activity against this organism.

To prevent postoperative infection in contaminated or potentially contaminated surgery, the recommended dose is a single 1gram IM or IV administered 30 to 90 minutes prior to start of surgery.

Cesarean Section Patients

The first dose of 1 gram is administered intravenously as soon as the umbilical cord is clamped. The second and third doses should be given as 1 gram 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 50 mg/kg per dose every 12 hours IV
1-4 weeks of age 50 mg/kg per dose every 8 hours IV

Infants and Children (1 month to 12 years):

For body weights less than 50 kg, the recommended daily dose is 50 to 180 mg/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 weights 50 kg or more, the usual adult dosage should be used; the maximum daily dosage should not exceed 12 grams.

CONTRAINDICATIONS:

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

WARNINGS:

• Before therapy with clafort 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. This product should be given with caution to patients with type I hypersensitivity reactions to penicillin. Antibiotics should be administered with caution to any patient who has demonstrated some form of allergy, particularly to drugs. If an allergic reaction to clafort occurs, discontinue treatment with the drug. Serious hypersensitivity reactions may require epinephrine and other emergency measures.

• Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including Cefotaxime, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of C. difficile. C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of C. difficile cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents. If CDAD is suspected or confirmed, ongoing antibiotic use not directed against C. difficile may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of C. difficile, and surgical evaluation should be instituted as clinically indicated.

PRECAUTIONS:

- Prescribing Cefotaxime in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.
- Cefotaxime 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 doses in patients with transient or persistent reduction of urinary output because of renal insufficiency, the total daily dosage should be reduced when Cefotaxime 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 are obtained, the dose of cefotaxime sodium be halved in patients with estimated creatinine clearances of less than 20 mL/min/1.73 m2.
- As with other antibiotics, prolonged use of Cefotaxime may result in overgrowth of nonsusceptible organisms. Repeated evaluation of the patient's condition is essential. If superinfection occurs during therapy, appropriate measures should be taken.
- As with other beta-lactam antibiotics, granulocytopenia and, more rarely, agranulocytosis may develop during treatment with Cefotaxime, particularly if given over long periods. For courses of treatment lasting longer than 10 days, blood counts should therefore be monitored.
- Cefotaxime, like other parenteral anti-infective drugs, may be locally irritating to tissues and may result in tissue damage and require surgical treatment. To minimize the potential for tissue inflammation, infusion sites should be monitored regularly and changed when appropriate.
- In the case of side effects such as dizziness the patient's ability to concentrate and to react properly may be impaired. In such cases the patients should refrain from driving cars and using machines.
- Positive Coombs test may occur during treatment with cephalosporins. This phenomenon may be encountered during treatment with cefotaxime.

DRUG INTERACTIONS:

- Increased nephrotoxicity has been reported following concomitant administration of cephalosporins and aminoglycoside antibiotics.
- Probenecid interferes with the renal tubular transfer of cefotaxime, decreasing the total clearance of cefotaxime by approximately 50% and increasing the plasma concentrations of cefotaxime. Administration of cefotaxime in excess of 6 grams/day should be avoided in patients receiving probenecid.
- Cephalosporins, including cefotaxime sodium, are known to occasionally induce a positive direct Coombs' test.

PREGNANCY:

Pregnancy Category B

There are no well-controlled studies in pregnant women. Because animal reproductive studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers

Cefotaxime is excreted in human milk in low concentrations. Caution should be exercised when Clafort is administered to a nursing woman.

Geriatric Use

This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function. weighed against the possible risks.

ADVERSE REACTIONS:

The most common adverse reactions have been local reactions following IM or IV injection. The reported adverse events are; Injection site inflammation with IV administration. Pain, induration and tenderness after IM injection. Rash, pruritus, fever, eosinophilia, colitis, diarrhea, nausea, vomiting, symptoms of pseudomembranous colitis, neutropenia, transient leukopenia, positive direct Coombs Tests during treatment with Cefotaxime and other cephalosporin antibiotics, moniliasis, vaginitis, headache, transient elevations in AST, ALT, serum LDH, serum alkaline phosphatase levels have been reported. As with some other cephalosporins, transient elevations of BUN have been occasionally observed with Cefotaxime.

The other reported adverse events are life-threatening arrhythmias, encephalopathy (e.g. impairment of consciousness, abnormal movements and convulsions), cases of toxic epidermal necrolysis, Stevens-Johnson syndrome, erythema multiforme, hemolytic anemia, agranulocytosis, thrombocytopenia, anaphylaxis (e.g., angioedema, bronchospasm, malaise possibly culminating in shock), urticaria, interstitial nephritis, transient elevations of creatinine, hepatitis, jaundice, cholestasis, elevations of gamma GT and bilirubin.

Superinfection, pancytopenia, dizziness, abdominal pain, hepatitis (sometimes with jaundice), exanthematous pustulosis and acute renal failures are also reported events.

OVERDOSAGE

The most frequent reactions were elevations of BUN and creatinine. There is a risk of reversible encephalopathy in cases of administration of high doses of beta-lactam antibiotics including cefotaxime. No specific antidote exists. Patients who receive an acute overdosage should be carefully observed and given supportive treatment.

Preparation of Clafort Injection

Strength	Diluent (mL)	Withdrawable Volume (mL)	Approx. (mg/mL) Concentration
250mg vial* (IM)	2	2	125
250mg vial* (IV)	2	2	125
500mg vial* (IM)	2	2.2	230
1g vial* (IM)	3	3.4	300
500mg vial* (IV)	10	10.2	50
1g vial* (IV)	10	10.4	95
2g vial* (IV)	10	11	180
1g infusion	50-100	50-100	20-10
2g infusion	50-100	50-100	40-20

(*) in conventional vial

Shake to dissolve; inspect for particulate matter and discoloration prior to use. Solutions of Clafort range from vary pale yellow to light amber, depending on concentration, diluent used, and length and condition of storage.

For intramuscular use: Reconstitute VIALS with Sterile Water for Injection.

For intravenous use: Reconstitute VIALS with at least 10 mL of Sterile Water for Injection. Reconstitute INFUSION BOTTLES with 50 or 100 mL of 0.9% Sodium Chloride Injection or 5% Dextrose Injection.

NOTE: Solutions of Clafort must not be admixed with aminoglycoside solutions. If Clafort and aminoglycosides are to be administered to the same patient, they must be administered separately and not as mixed injection.

For intermittent IV administration, a solution containing 1 gram or 2 grams in 10 mL 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.

PRESENTATION:

Clafort is supplied in the following dosage forms, strengths and pack sizes:

Clafort Injection 250mg IM/IV:
1 vial of 250mg Cefotaxime and 1 ampoule of 5ml water for injection.

Clafort Injection 500mg IM/IV:
1 vial of 500mg Cefotaxime and 1 ampoule of 10ml water for injection.

Clafort Injection 1g IM/IV:
1 vial of 1g Cefotaxime and 1 ampoule of 10ml water for injection.

Clafort Injection 2g IV:
1 vial of 2g Cefotaxime and 1 ampoule of 10ml water for injection.

DOSAGE & INSTRUCTIONS:

To be used on the prescription of a registered medical practitioner only.
Keep out of the reach of children.
Do not store above 30°C.
Protect from sunlight, heat and moisture.
Detailed prescribing information is available at **www.curexahealth.com**

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خوراک و ہدایات:
صرف مستند ڈاکٹر کے نسخہ کے مطابق ہی دوا استعمال کی جائے۔
بچوں کی پہنچ سے دور رکھیں۔ دوا کو 30°C سے زیادہ درجہ حرارت پر مت رکھیں۔
دھوپ، گرمی اور نمی سے محفوظ رکھیں۔

Manufactured by:
Curexa Health
Curexa Health Private Limited
Plot No. 517, Sundar Industrial Estate, Lahore - Pakistan

Ampoule Manufactured by:
SURGE LABORATORIES
10 K.M. Faisalabad Road, Bhikhi, District Sheikhupura-Pakistan

5130004

Marketed by:
H I G H N O O N
17.5 K.M. Multan Road, Lahore - Pakistan