[싱가포르][말레이시아]

세프악손주 설명서

Size : 110 × 300 (mm)

수정사항

1. ■DESCRIPTION 내용 수정
2. Product Registration Holder 추가
3. Date of revision 추가

Third Generation Cephalosporins

CEFAXONE

Ceftriaxone sodium

250mg, 500mg, 1g

INJECTION

■ COMPOSITION : Each vial contains

Ceftriaxone sodium ····· 250mg (potency)
····· 500mg (potency)
····· 1g (potency)

■ DESCRIPTION

CEFAXONE INJECTION is a white or light-yellow powder in a colorless transparent vial. Each box comes with 10vials and a package insert.

■ PHARMACOLOGY

Ceftriaxone possesses potent activity, both in vitro and in vivo, against a broad range of bacteria. MIC_{50} and MIC_{90} geometric means were calculated using the results of broth and agar dilution assays performed worldwide. The MIC_{90} for ceftriaxone overall was 8μg/ml or less for Enterobacteriaceae and 0.024μg/ml or less for Neisseria and Hemophilus species. Moderate activity was noted against eudomonas andetob-acterspecies (MIC_{50} 12 to 28μg/ml). Ceftriaxone was extremely active against nonenterococcal streptococci (MIC_{90} 0.07 μg/ml or less) and quite active against methicillin-susceptible Staphylococcus aureus(MIC_{90} 5μg/ml or less). Ceftriaxone generally was inactive against enterococci andmethicillin-resistant staphylococci. Activity against anaerobes was good, except for many strains of Bacteroides fragills and B. thetaiotaomicron (MIC greater than 64μg/ml). Ceftriaxone exhibited excellent stability to beta-lactamases. The effect of medium and inoculums on in vitro testing was minimal. Excellent activity was demonstrated in vivo. Against Enterobacteriaceae, nonenterococcal streptococci, and H. influenza, the PD_{50} in mice generally was less than 1mg/kg. S. aureusstrains responded moderately (mean PD_{50} 6.5mg/kg), whereas against most P.aeruginosa strains, PD_{50}s ranged from 5 to greater than 250mg/kg. The superiopharmacokinetic profile of ceftriaxone compared with that of other new cephalosporins was demonstrated by use of a prophylactic treatment schedule. The ability of ceftriaxone to penetrate the cerebrospinal fluid and provide excellent therapeutic coverage was confirmed in experimental meningitis models.

■ PHARMACOKINETICS

In human subjects, ceftriaxone exhibits an exceptionally long elimination half-life (5.8 to 8.7 hours) and a small degree of nonlinearity in its pharmacokinetics which can be ignored in its clinical applications. Thirty-three to 67 percent of a does is excreted in the urine as unchanged drug, and the remainder is secreted in the bile and ultimately is found in the feces as microbiologically inactive compounds. Ceftriaxone is rapidly and completely absorbed following intramuscular administration. Multiple dosing of ceftriaxone with doses ranging from 0.5 to 2g at 12 or 24 hour intervals by intravenous and intramuscular routes resulted in 15 to 36 percent accumulation of ceftriaxone in plasma and no change in its elimination half-life. The volume of distribution and the plasma clearance of ceftriaxone in pediatric were threefold greater than those in adults, and ceftriaxone penetrated the inflamed meninges of infants and children with bacterial meningitis. Small changes in the pharmacokinetics of ceftriaxone in elderly subjects or patients with renal or hepatic dysfunction are such that dose adjustments should not be necessary with a ceftriaxone dosage up to 2g per day. Ceftriaxone was not removed to any significant extent from plasma by hemodialysis. In a small percentage of patients, on dialysis, the elimination rate of ceftriaxone was significantly reduced, suggesting that plasma concentrations of ceftriaxone should be monitored in these patients to determine if dosage adjustments are necessary.

■ INDICATIONS

Spectrum of activity

Staphylococcus aureus (including penicillinase-producing strains), Staphylococcus epidermidis, Streptococcus pneumoniae, Streptococcus group A (Str. Pyogenes), Streptococcus group B (Str. aggalactiae), Streptococcus viridians group, Streptococcus bovis, Aeromonas spp., Alcaligenes spp., Branhamella catarrhalis, Citrobacter spp. ,Enterobacter spp. (some strains are resistant), Escherichia coli, Haemophilus ducreyi, Haemophilus influenzae (including amplicillin-resistant strains) Haemophilus parainfluenzae, Klebsiella spp., (including KI, pneumoniae), Moraxella spp., Proteus morgani, Proteus mirabilis, Proteus vulgaris, Providencia spp., Neisseria gonorrheae (including peniciallinase producing strains), Neisseria meningitides, Plesiomonas shigelloides, Pseudomonas aeuroginosa (some strains are resistant) Salmonella spp. (including S. typhi), Serratia spp. (including S. Marcescens), Shigella spp., Yersinia spp. (including Y. enterocolitica), Bacteroides spp.(including Y. enterolitica), Treponema pallidum, Bacteroides spp. (including some strains of B. fragilis), Clostridium spp. (except Cl. Difficile) Fusobacterium spp. (except F. mortiferum and F. varium), Peptococcus spp., Peptostreptococcus spp.

INDICATIONS

1. Main Indications

Respiratory tract infections such as pneumonia, bronchitis, etc., ear, nose and throat infections, renal and urinary tract infections, sepsis and meningitis perioperative and postoperative prophylaxis of infections, bones and joints infections, infections of skin, wounds and soft tissue, Abdominal infections(peritonitis, infections of biliary and gastrointestinal tract)genital infections such as gonorrhea, etc

2. Can be used in the following disease infections in immunosuppressed patients.

■ ADVERSE REACTIONS

1) Shock : As anaphylactic shock may rarely occur cautious monitoring is required, and in case that unpleasantness, stridor, dizziness, tenesmus, tinnitus, sweating, etc. occur further administration should be discontinued and appropriate measures taken.
2) Hypersensitivity : When eruption, urticaria, erythema, reddening, pruritis, chills, fever, allergic, dermatitis, edema, erythema, multiforme, anaphylactic or anaphylactoid reaction occur, futhur administration should be discontinued and appropriate measures taken. Severe dermal adverse reaction (erythema multiforme). Steven Johnson syndrome (muco-cutanec-ocular syndrome). Lyell syndrome (toxic epidermal necrolysis) may rarely occur.
3) Blood : Occasionally, agranulocytosis, granulocytopenia, eosinophilia, thrombocytosis, leukopenia, rarely anemia, hemolytic anemia, thrombocytopenia, prothrombin abnormality may occur.
4) Liver : Occasionally elevation of AST, ALT, AL-P and symptoms due to precipitation of ceftriaxone calcium salt in the gall-bladder, rarely elevation of bilirubin, γ-GTP may occur.
5) Kidney : As severe renal disorder such as acute renal failure has been reported to occur rarely, cautious observation such as periodic monitoring is required and if abnormality is acknowledged, further administration should be discontinued and appropriate measures taken. Very rarely, precipitation of the calcium salt of ceftriaxone in renal has been observed in children over 3 age precipitation in renal, which could caused renal insufficiency are symptomatic or asymptomatic. These effects resolved following discontinuance of the drug. In above case, high dosage (over 10 g/day) was administered to a patient who had a risk factor such as medicated over daily dosage, restricted water intake and mainly lain sick in bed.
6) GI system : Rarely severe enterocolitis with hemafecia such as pseudomembranous enterocolitis may occur. If abdominal pain and frequent diarrhea occur, appropriate measure such as immediate discontinuation of CEFAXONE, should be taken. Also occasionally nausea, vomiting, loose stools, diarrhea or rarely abdominal pain, anorexia, etc. may occur.
7) Respiratory system : Since interstitial pneumonia, PIE syndrome etc. accompanied with fever, cough, dyspnea, abnormal chest X-ray, eosinophilia, etc. may rarely occur with other cephems, in case that such symptoms occur, further administration should be discontinued and appropriate measures such as administration of corticosteroids, etc. should be taken.
8) Superinfection : Rarely, stomatitis and candidiasis may occur.
9) Vitamin deficiency : Rarely, symptoms of vitamin K deficiency (hypoprotherombinemia, hemorrhage tendency, etc.) and vitamin B deficiency (glossitis, stomatitis, anorexia, neuritis, etc.) may occur.
10) Others : Occasionally, headache and rarely vertigo, edema, precipitation in gallbladder, ventricular extrasystole, elevation of creatinine and mycosis in genital organ, etc.

■ UNDESIRABLE EFFECTS

Postmarketing Experience

Nervous system disorders: encephalopathy

Reversible encephalopathy has been reported with the use of cephalosporins, including ceftriaxone, particularly when high doses are administered in patients with renal impairment and additional predisposing factors such as older age, pre-existing central nervous system disorders.

■ CONTRAINDICATIONS

1) Patients with history of shock to ceftriaxone sodium.
2) Patients with hypersensitivity to cephalosporins.
3) Patients with hypersensitivity or history of hypersensitivity to penicillins.

■ PRECAUTIONS

1. In order to prevent appearance of the resistant microorganisms, susceptibility should be determined and treatment should be continued only for the minimum period of time required.
2. In order to predict adverse reaction such as shock, etc. patient history should be checked in detail and skin reaction test should be performed.
3. Emergency facilities should be prepared in case of the development of shock. (if anaphylactic shock occurs intravenous epinephrine has to be followed by a glucocorticoid injection). After administration, patients should be kept quiet and under adequate supervision.
4. It is desirable to perform laboratory test (hepatic function, renal function, blood etc.) at regular intervals during treatment.
5. Shadows which have mistaken for gallstones have been detected on sonograms of the gallbladder, usually following doses higher than the standard recommended dose. These shadows are however, precipitates of ceftriaxone calcium which disappear on completion or discontinuation of CEFAXONE therapy. Rarely, these findings have been associated with symptoms. In symptomatic cases, conservative non-surgical management is recommended. Discontinuation of CEFAXONE treatment in symptomatic cases should be at the discretion of the clinician.
6. a) Pseudomemberanous colitis has been reported with nearly all antibacterial agents, including ceftri-

axone, and may range in severity from mild to life-threatening. Therefore, it is important to consider the diagnosis in patients who present with diarrhea subsequent to the administration of antibacterial agent.
b) Prolonged use of CEFAXONE may result in overgrowth of non-susceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.

7. CEFAXONE is not reported to have adverse effect on a person's ability to drive vehicles or operate machinery.
8. Careful administration
1) Patients with history of drug allergy
2) Patients oneself of whose parents, sisters or brothers are prone to suffer from allergic symptoms such as bronchial asthma, exanthema, urticaria, etc.
3) Patients with severe renal disorder(as the plasma concentration is maintained for a long period of time, decreased dosage or increased interval between treatments are required)
4) Patients with poor oral or parenteral nutrition patients, elderly patients, patients with poor general conditions (Cautious monitoring is required since vitamin K deficiency may occur).
9. Interference with laboratory test.
1) Caution should be taken as urine-glucose test using Benedict's reagent Fehling's reagent, Clinitest, except for Testape reaction, may give false positive results.
2) Caution should be taken as direct Cooms-test may give false positive results.
3) CEFAXONE like other antibiotics may result in false-positive tests for galactosemia.
10. Precautions on application
1) As vascular pain, venous thrombosis, flushing, nausea, vomiting may rarely occur by large intravenous dose, caution should be taken on preparation of injectable solution, site of injection, method of administration, etc., and infection should be given as slowly as possible.(i.v injection)
2) CEFAXONE should be used immediately after reconstitution. Particularly, caution should be taken when dissolving in glutathione preparation or high concentration amino acid solution.

■ DRUG INTERACTION

1. No impairment of renal function has so far been observed after concurrent administration of large doses of CEFAXONE and potent diuretic (e.g frusemide)
2. Synergy between CEFAXONE and aminoglycosides has been demonstrated with many Gram-negative bacilli under experimental conditions and it is of special importance in severe life-threatening infections due to microorganisms such as Pseudomonas aeruginosa. Because of physical incompatibility the two drugs must be administered separately at the recommended dosages. There is no evidence that CEFAXONE increases renal toxicity of aminoglycosides.
3. No effect similar to that of disulfiram has been demonstrated after ingestion of alcohol subsequent to the administration of CEFAXONE.
4. The elimination of CEFAXONE is not altered by probenecid.
5. CEFAXONE does not contain an N-methylthiotetrazole moiety associated with possible ethanol intolerance and bleeding problems of certain other cephalosporins.
6. In an in vitro study antagonistic effects have been observed with the combination of chloramphenicol and ceftriaxone.

■ DOSAGE AND ADMINISTRATION

1. Adults and children over twelve years : 1~2g (potency) of ceftriaxone sodium is administered once daily intravenously or intramuscularly. In severe case or infections caused by moderately sensitive organisms, the dosage may be increased up to 4g (potency) once daily.
2. Neonates (14 days or below) : A daily dose is 20~50 mg (potency)/kg bodyweight is administered once a day and not to exceed 50mg (potency)/kg. It is not necessary to differentiate between premature and infants born at term.
3. Infants and children (15 days to twelve years) : daily dose of 20~80mg (potency)/kg is administered once a day. For children of 50 kg bodyweight or more, the usual adult dosage should be used. Intravenous doses of 50mg (potency)/kg or more should be given by infusion over at least 30minutes.
4. Elderly patients : In elderly patients, the dosages recommended for adults can be used without modification.
5. Meningitis : In bacterial meningitis in infants and children, treatment begins with doses of 100 mg (potency) / kg (not to exceed 4 g (potency)) once daily. As soon as the causative organism has been identified and its sensitivity determined, the dosage can be reduced accordingly.
The following duration of therapy has shown to be effective

Neisseria meningitidis	4 days
Haemophilus influenzae	6 days
Streptococcus pneumoniae	7 days

6. Gonorrhea : For the treatment of gonorrhea (penicillinase-producing and nonpenicillinase-producing strains), a single i.m. dose of 250 mg (potency) is recommended.
7. Perioperative and postoperative prophylaxis : To prevent postoperative infection in contaminated or potentially contaminated surgery, the recommended approach is single dose of 1~2g (potency) administered 30~90 minutes prior to surgery depending on the risk of infection. In colorectal surgery, concurrent (but separately administered) administration of CEFAXONE with or without 5-nitromidazole (e.g.ornidazole) has proven effective.
8. Impaired renal and hepatic function : In patients with impaired renal function, there is no need to reduce the dosage of CEFAXONE if hepatic function is intact, but in case of preterminial renal failure (creatinine clearance <10ml/min>) the dosage should not exceed 2g (potency) daily. In patients with liver damage, there is no need for the dosage to be reduced if renal function is intact. In cases of combined severe renal and hepatic dysfunction, the plasma concentration of the ceftriaxone should be measured at regular intervals. In patients undergoing dialysis, no additional supplementary dosing is required after the dialysis. Serum concentrations should be monitored, however, to determine whether dosage adjustment is necessary, since the elimination rate in these patients may be reduced.

○ Duration of therapy

The duration of therapy varies according to the recovery from the disease. In general, as with other antibiotic therapy, administration of the Cefaxone should be continued for a minimum of 48 to 72 hours after the patient has become afebrile or evidence of bacterial eradication has been obtained.

○ Preparation of injectable soultion

1. Intramuscular injection : For i.m. injection, CEFAXONE 0.25g or 0.5g is dissolved in 2ml and CEFAXONE 1 g in 3.5 ml of 1% lidocaine hydrochloride solution and injected deeply in the gluteal region. It is recommended that not more than 1g is injected at one site. I.m injection without lidocaine solution is painful. The lidocaine solution must never be administered intravenously.
2. Intravenous injection : For I.V. injection, CEFAXONE 0.25 g or 0.5 g is dissolved in 5ml, and CEFAXONE 1g in 10 ml sterile water for injection. The intravenous administration should be given over two to four minutes. In case of intravenous infusion, the infusion should last at least 30 minutes. For i.v. infusion, 2 g of CEFAXONE is dissolved in 40 ml of one of the following calcium-free infusion solutions, sodium chloride 0.9%, sodium chloride 0.45%+dextrose 2.5%, dextrose 5%, dextrose 10%, dextran 6% in dextrose 5%, hydroxyl ethyl starch 6~10% infusions or sterile water for injection. CEFAXONE solutions should not be mixed with or piggybacked into solutions containing other antimicrobial drugs or into diluent solutions other than those listed above, owing to possible incompatibility.
Reconstituted solutions retain their physical and chemical stability for six hours at room temperature or 24 hours at 5℃. As a general rule however, the solutions should be used immediately after reconstitution. Reconstituted solution has color ranging from pale yellow to amber, depending on the concentration and the length of storage. This characteristic of the active ingredient is of no significance for the efficacy or tolerance of the drug.

■ SYMPTOMS & TREATMENT OF OVERDOSAGE

In the case of overdosage, drug concentration would not be reduced by hemodialysis or peritoneal dialysis. There is no specific antidote. Treatment of overdosage should be symptomatic.

■ USE IN PREGANANCY, LACTATION & NEONATES

Pregnancy
1) CEFAXONE permeates placenta.
2) As safety in human pregnancy has not been established, CEFAXONE should not be administered to pregnant women or women of child bearing potential unless therapeutic benefit is considered to exceed the possible risk.
Lactation
As CEFAXONE is excreted in the breastmilk at low concrentration, caution is advised in nursing mothers. Neonates and Prematures.
1) Safety on neonates and prematures has not been established.
2) Studies have shown that ceftriaxone, like some other cephalosporins, can displace bilirubin from serum albumin. Caution should be excercised when considering CEFAXONE treatment in hyperbilirubimrmic neonates. CEFAXONE should not be used in neonates (especially prematures) at risk of developing bilirubin encephalopathy.

■ **INCOMPATIBILITIES** : Calcium containing solution or with aminoglycosides, fluconazole, vancomycin or amsacrine.

■ **STORAGE** : Store in a hermetic container below 30℃

■ HOW SUPPLIED

0.25 g/Vial × 10, 0.5 g/Vial × 10, 1 g/Vial × 10

■ **SHELF LIFE** : 3years from the manufacture date

Product Registration Holder:
The Zyfas Medical Co.
No 15, Jalan Mega 1/5,
Taman Perindustrian Nusa Cemerlang,
79200 Iskandar Puteri,
Johor, Malaysia

Date of revision:
April. 8, 2024

SHIN POONG PHARM. CO., LTD.
41-15, Osongsaengmyeong 5-ro, Osong-eup, Heungdeok-gu,
Cheongju-si, Chungcheongbuk-do, Republic of Korea