

Bestrix

(Ceftriaxone Sodium U.S.P.)

INJECTION

انجکشن

بیسٹرکس

(سیفٹرائزن سولفیم یو.ایس.پی.)

COMPOSITION:

Each I.V. vial of 250mg, 500mg & 1000mg contains:
Ceftriaxone (as Ceftriaxone Sodium) 250mg, 500mg & 1000mg respectively.
Each I.M. vial of 250mg, 500mg contains:
Ceftriaxone (as Ceftriaxone Sodium) 250mg, 500mg respectively.
Product Specs.: U.S.P.

DESCRIPTION:

Ceftriaxone is a long acting, 3rd generation cephalosporin antibiotic for parenteral use.

MODE OF ACTION:

Ceftriaxone inhibits bacterial cell wall synthesis by blocking transpeptidation of peptidoglycan. Ceftriaxone activates autolytic enzymes in the cell wall, which results in lesions that cause bacterial death.

CLINICAL PHARMACOLOGY:

Ceftriaxone is reversibly bound to albumin. Half-life ranged from 5.8 to 8.7 hours. Bioavailability after intramuscular injection is 100%. It has shown excellent tissue and body fluid penetration. Concentrations, well above the MICs of most pathogens are detectable for more than 24 hours in over 60 tissues or body fluids including lung, heart, biliary tract/liver, tonsils, middle ear and nasal mucosa, bone, and cerebrospinal, pleural, prostatic and synovial fluids. It penetrates the inflamed as well as non inflamed meninges. Ceftriaxone crosses the placental barrier and is secreted in the breast milk at low concentrations.

ELIMINATION:

Ceftriaxone is not metabolized systemically; only the intestinal flora transforms the agent into inactive metabolites. 50-60% of ceftriaxone is excreted unchanged in the urine, while 40-50% is excreted unchanged in the bile.

PHARMACOKINETICS IN SPECIAL CLINICAL SITUATIONS:

In the first week of life, 80% of the dose is excreted in the urine; over the first month, this falls to levels similar to those in the adult. In elderly persons aged over 75 years, the average elimination half-life is usually 2 to 3 times longer than in the young adult group. Evidence gathered to date with ceftriaxone, however, suggests that no modification of the dosage regimen is needed.

RENAL OR HEPATIC DYSFUNCTION:

In patients with renal or hepatic dysfunction, the pharmacokinetics of ceftriaxone are only minimally altered and the elimination half-life is only slightly increased. If kidney function alone is impaired, biliary elimination of ceftriaxone is increased; if liver function alone is impaired, renal elimination is increased.

MICROBIOLOGY:

Ceftriaxone has a high degree of stability in the presence of beta-lactamases, both penicillinases and cephalosporinases of gram-negative and positive bacteria. Ceftriaxone is usually active against the following microorganisms in vitro & in clinical infections.

Gram-positive Aerobes

Str. Pneumoniae	Str. Viridins
Streptococci, group A (including Str. pyogenes)	Str. bovis (group D, non-enterococci)
Streptococci, group B (including Str. agalactiae)	St. aureus

NOTE: Methicillin-resistant staphylococci are resistant to cephalosporins, including ceftriaxone. Most strains of Group D streptococci and *Enterococcus faecalis*, *Enterococcus faecium* and *Listeria monocytogenes* are resistant.

Gram-negative Aerobes:

H. influenzae (including ampicillin resistant strains)	Enterobacter species
H. parainfluenzae	S. marcescens
N. meningitidis	Citrobacter species
N. gonorrhoea (including ampicillin resistant strains)	P. mirabilis
E. coli	Proteus indole-positive (including Morganella morganii)
Klebsiella species	Salmonella species
	Shigella species

Anaerobic Organisms:

Bacteroides spp (including some strains of B. fragilis)	Peptostreptococcus spp
Fusobacterium spp	Peptococcus spp
	Clostridium spp (except Cl. difficile)

PATHOGEN WHICH DO NOT RESPOND TO CEFTRIAZONE:

● Ureaplasma urealyticum	● Mycobacterium sp.
● Mycoplasma sp.	● Fungi

INDICATIONS:

Ceftriaxone is indicated for the treatment of the following infections when caused by susceptible organisms:

- Respiratory Tract Infections (particularly pneumonia, ear, nose and throat infections)
- Skin and Skin Structure Infections
- Urinary Tract Infections (complicated and uncomplicated)
- Uncomplicated Gonorrhea (cervical/urethral and rectal)
- Pelvic Inflammatory Disease caused by *Neisseria gonorrhoeae*.
- Chancroid
- Bacterial Septicemia
- Bone and Joint Infections
- Intra-Abdominal Infections (peritonitis, infections of the biliary and gastrointestinal tracts)
- Meningitis and other CNS infections
- Endocarditis
- Typhoid fever and other infections caused by *Salmonella*.
- Lyme disease
- Empiric anti-infective therapy in febrile neutropenic patients
- Perioperative prophylaxis

DOSEAGE AND ADMINISTRATION:

Adults and Children over twelve years:

The usual adult daily dose is 1 to 2 grams given once a day (or in equally divided doses twice a day) depending on the type and severity of infection. The total daily dose should not exceed 4 grams.

Elderly patients:

The dosages recommended for adults require no modification in the case of geriatric patients.

Neonates, Infants and Children up to twelve years:

The following dosage schedules are recommended for once daily administration:

Neonates (up to 14 days):

A daily dose of 20-50mg/kg bodyweight, not to exceed 50mg/kg

Infants and children (15 days to twelve years):

A daily dose of 20-80 mg/kg body weight, depending on the severity of infection, usually at 24 hr intervals. Intravenous doses of 50mg or more per kg should be given by infusion over at least 30 minutes. The total daily dose should not exceed 2 grams.

COMBINATION THERAPY:

Synergy between ceftriaxone and aminoglycosides has been demonstrated with many Gram-negative bacilli under experimental conditions. Although enhanced activity of such combinations is not always predictable, it should be considered in severe, life-threatening infections due to microorganisms such as *Pseudomonas aeruginosa*. Because of physical incompatibility the two medicines must be administered separately at the recommended dosages.

SPECIAL DOSAGE INSTRUCTIONS:

Meningitis:

In bacterial meningitis in infants and children, treatment begins with doses of 100mg/kg (not to exceed 4g) once daily. As soon as the causative organism has been identified and its sensitivity determined, the dosage can be reduced accordingly. The usual duration of therapy is 7 to 14 days. The best results have been found with the following duration of therapy:

<i>Neisseria meningitidis</i>	4 days	<i>Streptococcus pneumoniae</i>	7 days
<i>Haemophilus influenzae</i>	6 days		

Acute bacterial otitis media:

A single intramuscular dose of 50 mg/kg (not to exceed 1 gram) is recommended.

Gonorrhoea:

A single IM dose of 250mg ceftriaxone is recommended.

Perioperative prophylaxis:

To prevent postoperative infections in contaminated or potentially contaminated surgery, the recommended approach - depending on the risk of infection - is a single dose of 1-2g administered 30-90 minutes prior to surgery. In colorectal surgery, concurrent (but separate) administration of ceftriaxone with or without a 5-nitroimidazole, e.g. ornidazole, has proven effective.

IMPAIRED RENAL & HEPATIC FUNCTION:

In patients with impaired renal function, there is no need to reduce the dosage of ceftriaxone provided hepatic function is intact. Only in cases of preterminal renal failure (creatinine clearance <10 mL/min) should the ceftriaxone dosage not exceed 2g daily. In patients with liver damage, there is no need for the dosage to be reduced provided renal function is intact. In cases of concomitant severe renal and hepatic dysfunction, the plasma concentrations of ceftriaxone should be determined at regular intervals.

In patients undergoing dialysis no additional supplementary dosing is required following the dialysis.

DIRECTION FOR USE:

Reconstituted solutions retain their physical and chemical stability for six hours at room temperature (or 24 hours at 2-8°C).

As a general rule, however the solution should be used immediately after preparation. They range in colour from pale yellow to amber, depending on the diluent used, concentration and the length of storage.

Intravenous injection:

For IV injection, ceftriaxone 250mg or 500mg is dissolved in 5mL, and ceftriaxone 1g in 10mL of sterile water for injections. The intravenous administration should be given over 2 to 4 minutes.

Intramuscular Injection:

For IM injection, ceftriaxone 250mg or 500mg is dissolved in 2mL & 1g in 3.5mL of 1% lidocaine HCl solution and injected well within the body of a relatively large muscle. It is recommended that not more than 1g to be injected at one site.

The lidocaine solution must never be administered intravenously.

Intravenous infusion:

The infusion should last at least 30 minutes.

For IV infusion, 2g ceftriaxone is dissolved in 40mL 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%, hydroxyethyl starch 6-10% infusions, sterile water for injections. Ceftriaxone solutions should not be mixed with solutions containing other antimicrobial drugs or into diluent solutions other than those listed above, owing to possible incompatibility.

PREGNANCY:

Pregnancy Category B

SIDE EFFECTS:

Ceftriaxone is generally well tolerated. In clinical trials, the following adverse reactions, which were considered to be related to Ceftriaxone therapy or of uncertain etiology, were observed:

Local Reactions: pain, induration and tenderness was 1% overall. Phlebitis was reported in <11% after IV administration. The incidence of injection site reaction was 17% (3/17) after IV administration of 350 mg/mL and 5% (1/20) after IM administration of 250 mg/mL.

Hypersensitivity: rash (1.7%). Less frequently reported (<1%) were pruritus, fever or chills. **Hematologic:** eosinophilia (6%), thrombocytosis (5.1%) and leukopenia (2.1%). Less frequently reported (<1%) were anemia, hemolytic anemia, neutropenia, lymphopenia, thrombocytopenia and prolongation of the prothrombin time.

Gastrointestinal: diarrhea (2.7%). Less frequently reported (<1%) were nausea or vomiting, and dysgeusia. The onset of pseudomembranous colitis symptoms may occur during or after antibacterial treatment. **Hepatic:** elevations of SGOT (3.1%) or SGPT (3.3%). Less frequently reported (<1%) were elevations of alkaline phosphatase and bilirubin.

Renal: elevations of the BUN (1.2%). Less frequently reported (<1%) were elevations of creatinine and the presence of casts in the urine.

Central Nervous System: headache or dizziness were reported occasionally (<1%).

Genitourinary: moniliasis or vaginitis were reported occasionally (<1%).

Miscellaneous: diaphoresis and flushing were reported occasionally (<1%). Other rarely observed reactions (<0.1%) include leukocytosis, lymphocytosis, monocytosis, basophilia, a decrease in the colitis, flatulence, dyspepsia, palpitations and epistaxis.

CONTRAINDICATIONS:

- 1 Combined renal and hepatic dysfunction.
- 2 Hyperbilirubinemia.
- 3 Neonates (especially premature) at risk of developing bilirubin encephalopathy.
- 4 Hypersensitivity to ceftriaxone or to any of the cephalosporins.
- 5 ceftriaxone should not be used in pregnancy (particularly in the first trimester) unless absolutely indicated.

INTERACTIONS:

- 1 No impairment of renal function has so far been observed after concurrent administration of large doses of ceftriaxone and potent diuretics (e.g. frusemide).
- 2 There is no evidence that ceftriaxone 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 ceftriaxone.
- 4 The elimination of ceftriaxone is not altered by probenecid. In an in vitro study antagonistic effects have been observed with the combination of chloramphenicol and ceftriaxone.

PRECAUTIONS:

- 1 Hypersensitivity reactions may occur in susceptible individuals.
- 2 Pseudomembranous colitis has been reported with nearly all antibacterial agents including ceftriaxone. Therefore, it is important to consider this diagnosis in patients who present with diarrhoea subsequent to the administration of antibacterial agents.
- 3 Although transient elevations of BUN and serum creatinine have been observed, at the recommended dosages, the nephrotoxic potential of ceftriaxone is similar to that of other cephalosporins.
- 4 Prolonged use of ceftriaxone may result in overgrowth of nonsusceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.
- 5 Alterations in prothrombin times have occurred rarely in patients treated with ceftriaxone.
- 6 ceftriaxone should be prescribed with caution in individuals with a history of gastrointestinal disease, especially colitis.
- 7 Shadows which have been 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 calcium ceftriaxone which disappear on completion or discontinuation of ceftriaxone therapy.
- 8 During prolonged treatment the blood profile should be checked at regular intervals.

PRESENTATION:

Bestrix 250mg I.M.	1's with 2mL Lidocaine HCl
Bestrix 500mg I.M.	1's with 2mL Lidocaine HCl
Bestrix 250mg I.V.	1's with 5mL Water for injections
Bestrix 500mg I.V.	1's with 5mL Water for injections
Bestrix 1000mg I.V.	1's with 10mL Water for injections

DOSEAGE

As directed by the physician.

INSTRUCTIONS

Store below 30°C.
Protect from sunlight & moisture.
Keep out of reach of children.

Detailed prescribing information is available on request.

Manufactured by:

PharmEvo (Private) Ltd.
Plot # A-29, North Western
Industrial Zone, Port Qasim,
Karachi-75020

خوراک:

ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

ہدایات:

دوا کو 30°C سے کم درجہ حرارت پر رکھیں۔

دھوپ اور نمی سے بچائیں۔

بچوں کو پہنچنے سے دور رکھیں۔

