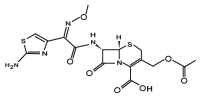
Yorker® 250mg/500mg/1g Injection

(Cefotaxime Sodium)

DESCRIPTION:

Yorker® contains cefotaxime, belongs to the class of drugs called third generation cephalosporins, creamy white 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

Structural Formula



COMPOSITION:

Yorker® **250mg injection:** Each vial contains: Sterile powder of Cefotaxime sodium USP equivalent to Cefotaxime.....250mg

Yorker® **500mg injection:** Each vial contains: Sterile powder of Cefotaxime sodium USP equivalent to Cefotaxime..... 500mg

Yorker® **1g injection:** Each vial contains: Sterile powder of Cefotaxime sodium USP equivalent to Cefotaxime.....1g

PHARMACOLOGY:

Mechanism of Action

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

PHARMACOKINETICS:

IM Injection

Following IM injection of doses of 250mg, 500mg and 1g, peak levels were recorded at 30 minutes. The level increased according to the dose and was approximately 24 µg/ml after the 1g injection. Urinary excretion in the 24 hours after injection was 50 - 60% of the dose administered. It was 44 - 55% in the first 6 hours after IM Injection. The serum protein binding of the drug was approximately 38%

IV Injection

The initial phase half-lives for whole blood and plasma are 4.5 and 8 minutes respectively. Terminal phase half-lives for whole blood and plasma are 1.3 and 2.2 hours respectively. 85 to 90% of the administered dose is excreted in the urine and 7 - 9.5% in the faeces. Most of the dose is excreted within 4 hours of dosing. Approximately 20 - 36% of an IV administered dose of cefotaxime is excreted by the kidney as unchanged cefotaxime and 15 - 25% as the desacetyl derivative, the major metabolite. Desacetylcefotaxime has been shown to contribute to the bactericidal activity. Two other urinary metabolites (M2 & M3) account for 20 - 25%. They lack bactericidal activity. After a single IV injection of Yorker® 1g serum protein binding of the drug is approximately 44%

IV Infusion

Loading dose of 500mg, 1g and 2g administered over 15 minutes followed by sustaining infusions of 0.5g, 1g and 2g per hour produces mean peak serum levels of 41.93 and 160µg/ml respectively. The mean terminal half-life 75±7 minutes. 63±9% of the administered dose is excreted through the kidneys within 24 hours. Serum protein binding is approximately 35%

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 multiple 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
- Fusobacterium spp. (Including Fusobacterium nucleatum)
- Peptostreptococcus spp.
- Clostridium spp. (**Note:** Most strains of Clostridium difficile are resistant)
- Peptococcus spp.

Cefotaxime sodium also demonstrates in vitro activity against the following microorganisms but the clinical significance is unknown. Cefotaxime sodium exhibits in vitro minimal inhibitory concentrations (MIC's) of 8mcg/ml or less against most (90%) strains of the treating clinical infections due to these microorganisms have not been established in adequate and well-controlled clinical trials

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

INDICATIONS & USAGE:

Yorker® is indicated for use primarily in the treatment of infections of the genitourinary, gastrointestinal and respiratory tracts, in the skin and soft tissues and meningitis in children caused by susceptible strains of the following organisms:

Staphylococcal infections: (Including infections caused by both penicillinase-producing and non-penicillinase-producing strains): abscess, furunculosis, bronchitis and impetigo

Streptococcal infections: (Both ß-haemolytic and group D streptococci), cellulitis, pneumonia, follicular tonsillitis, otitis media, pharyngitis, sinusitis, scarlet fever, septic sore throat, urinary tract infections (Enterococci) and meningitis in children

Pneumococcal infections: Lobar pneumonia, bronchitis, cellulitis and otitis media

Haemophilus influenzae infections: Otitis media, laryngotracheobronchitis and meningitis in children

E. coli infections: Labor pneumonia, urinary tract infections and meningitis in children

Shigella infections: Bacillary dysentery

Salmonella infection: Enteritis

Sensitive strains of Pseudomonas aeruginosa: Sepsis

Gonococcus: Gonorrhoea

Neisseria Meningitidis: Meningitis in children

Bacteriological studies to determine the causative organisms and their sensitivity to Yorker® should be performed

Prophylactic uses

The administration of Yorker® perioperatively may reduce the incidence of certain post-operative infections in patients undergoing surgical procedures that are classified as potentially contaminated

The minimum effective dose has been found to be 1g Yorker® 30-90 minutes prior to surgery

CONTRA-INDICATIONS:

Yorker® is contra-indicated in subjects allergic to cephalosporins

Warning

Yorker® must be used with caution in penicillin-sensitive subjects. Strict medical supervision is required throughout the treatment

DOSAGE AND DIRECTIONS FOR USE:

Intravenous and Intramuscular Injections

Dissolve Yorker® in water for injection USP as shown below. Shake well until dissolved and then withdraw the entire contents of the vial into the syringe and use immediately

Vial size	Volume of water for injection to be added
250mg	2ml
500mg	2ml
1g	4ml

Intravenous Infusion

Yorker® may be administered by intravenous infusion using 1g vials. 1 - 2g are dissolved in 40 - 100ml of water for injection USP or in the infusion fluids listed under "Stability in Infusion Fluids"

The prepared infusion solutions should be administered over 20 - 60 minutes

Dosage, route of administration and frequency of injections depend on the nature and severity of the infection, the condition of the patient, and the sensitivity of the pathogens to cefotaxime

Adults

Usual dose 2g daily, in 2 x 1g injections. Severe cases may be given 3 - 4g daily in 2 - 4 administrations. Very severe cases may be given up to 12g IV

Neonates, Infants and Children

Neonates

The following dosage schedule is recommended:

0 - 1 week of age - 50mg/kg IV q 12 hrs.

1 - 4 weeks of age - 50mg/kg IV q 8 hrs.

Infants and Children

Usual daily dose 50 - 100mg/kg body mass in 2 - 4 injections. In exceptional cases up to 200mg/kg per day may be given

In Renal Failure

The dosage of Yorker® should be reduced by half in patients with creatinine clearances of less than 20 ml/minute. The dosage interval should not be modified

OR

As directed by the physician

WARNING:

Use freshly prepared solution. Do not mix Yorker® with another antibiotic in the same syringe or infusion

Stability in infusion fluids

The stability of Yorker® in a concentration of 1g per 250 ml in the following infusion fluids is satisfactory for 24 hours in a refrigerator or 12 hours at a temperature not exceeding 22°C

0.9% Sodium chloride, 5% dextrose, Ringer's solution

SIDE-EFFECTS AND SPECIAL PRECAUTIONS:

It has not yet been established whether the product is safe in pregnancy, although animal studies have not shown any teratogenic effects

PRECAUTIONS:

- Stop the treatment should any allergic reaction appear
- Adapt the dosage in cases of organic or functional renal failure as mentioned under "Dosage and Directions for Use"
- Any combination with potentially nephrotoxic drugs and powerful diuretics should be taken into account in assessing the risks involved in such drug combinations

SIDE EFFECTS:

Local Reactions

Deep phlebitis after IV injection has been reported

General Reaction

Skin eruptions, fever, eosinophilia, neutropenia, transient leucopenia and haemolytic anaemia. Granulocytopenia and agranulocytosis may develop during treatment with cefotaxime, particularly if given over long periods. For cases of treatment lasting longer than ten days, blood counts should therefore be monitored. Cases of diarrhoea have been recorded. The onset of diarrhoea may indicate the appearance of Pseudomembraneous colitis, the diagnosis of which should be confirmed by colonoscopy. This occurrence requires immediate cessation of administration and treatment with appropriate specific antibiotic therapy. Temporary elevation of transaminases and alkaline phosphatases have been recorded

Interaction with Laboratory Tests

A false positive reaction can occur on testing for glucose in the urine with reducing substances, but this can be avoided with use of methods that are specific to gluco-oxidase

Development of a positive Coombs'test may occur during treatment with cefotaxime

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

Treatment should be symptomatic and supportive

In case of overdose, especially in renal impairment, there is a risk of reversible metabolic encephalopathy

AVAILABILITY:

Yorker® 250mg injection in a pack of 1 x 250mg vial + 5ml sterile water for injection

Yorker® 500mg injection in a pack of 1 x 500mg vial + 5ml sterile water for injection

Yorker® 1g injection in a pack of 1 x 1g vial + 5ml sterile water for injection

STABILITY:

See expiry on the pack

INSTRUCTIONS:

Keep out of reach of children. Avoid exposure to heat, light and humidity

Store between 15 to 30°C. Improper storage may deteriorate the medicine

یورکر® ۲۵۰ ملی گرام / ۵۰۰ ملی گرام / ۱ گرام انجکشن

(سیفوٹیکزائم سوڈیم)

برائے عضلاتی / وریدی استعمال

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں

ہدایات: بچوں کی پہنچ سے دور رکھیں

دوا کو دھوپ، گرمی اور نمی سے محفوظ ۱۵ سے ۳۰ ڈگری سینٹی گریڈ کے درمیان رکھیں ورنہ دوا خراب ہو جائیگی

Manufactured by:

Healthtek (Pvt.) Limited
Plot No.14, Sector 19, Korangi
Industrial Area Karachi - Pakistan

Associate of:
SAMI Pharmaceuticals (Pvt.) Ltd.
Karachi-Pakistan
www.samipharmapk.com

P000929

R.N-01/HA/03/15/Pampac