SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE PRODUCT

Yorker® **(Cefotaxime Sodium) 250mg Injection**

Yorker® **(Cefotaxime Sodium) 500mg Injection**

Yorker® **(Cefotaxime Sodium) 1g Injection**

2. QUALITATIVE AND QUANTITATIVE 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

3. PHARMACEUTICAL FORM

Powder for solution for Injection

Appearance: Off-white to pale yellow crystalline powder free from visible particle.

4. CLINICAL PARTICULARS

4.1. THERAPEUTIC INDICATIONS:

Yorker® is indicated for the treatment of the following severe infections when known or thought very likely to be due to bacteria that are susceptible to cefotaxime:

- Bacterial pneumonia
- Complicated infections of the kidneys and upper urinary tract
- Severe infections of the skin and soft tissue
- Genital infections including Gonorrhoea
- Intra-abdominal infections (such as peritonitis)
- Acute bacterial meningitis
- Treatment of patients with bacteraemia that occurs in association with, or is suspected to be associated with, any of the infections listed above.

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2. POSOLOGY AND METHOD OF ADMINISTRATION:

Posology:
Cefotaxime may be administered by IV or IM, after reconstitution of the solution according to the directions given below. Dosage and mode of administration should be determined by the severity of the infection, susceptibility of the causative organism and the patient's condition. Therapy may be started before the result of sensitivity tests are known. Cefotaxime has synergistic effects with aminoglycosides.
Adults and children over 12 years: The usual dose in adults is 2 to 6g daily. The daily dosage should be divided. However, dosage may be varied according to the severity of the infection, sensitivity of causative organisms and condition of the patient.
Guidelines for dosage: ***Typical infection in presence (or suspicion) of a sensible micro-organism:*** 1g every 12 hours corresponding to a total daily dosage of 2g intramuscularly or intravenously. ***Infection in presence (or suspicion) of sensible or moderately sensible multiple microorganisms:*** 1-2g every 12 hours corresponding to a total daily dosage of 2 - 4g. ***Severe infection by unidentified micro-organisms or for infections that cannot be localised:*** 2-3g as a single dose every 6 to 8 hours up to a maximum daily dosage of 12g. A combination of Cefotaxime and other antibiotics is indicated in severe infections.
Infants and children (1 month to 12 years of age): The usual dosage for infants and children is < 50kg is 50-150mg/kg/day in 2 to 4 divided doses. In very severe infections up to 200mg/kg/day in divided doses may be required. In infants and children >50kg the usual dose in adults, without exceeding the maximum daily dose of 12g should be given.
New born infants and premature infants: The recommended dosage is 50mg/kg/day in 2 to 4 divided doses. In case of life-threatening situations, it may be necessary to increase the daily dose. In severe infections 150 – 200mg/kg/day have been given: In those situations, the following table may serve as a guide, since there are differences in kidney maturation.

Age	Daily dose of Cefotaxime
0-7 days	50mg/kg every 12h
8 days – 1 month	50mg/kg every 8h

Elderly: No dosage adjustment is required, provided that renal and hepatic function are normal.
Other recommendations: ***Gonorrhoea:*** For gonorrhoea, a single injection (intramuscularly or intravenously) of 0.5 g to 1g Cefotaxime. For complicated infections consideration should be given to available official guidance. Syphilis should be excluded before initiating the treatment. ***Urinary tract infections:*** In uncomplicated UTI 1g every 12 hours. ***Bacterial meningitis:*** In adults daily doses of 6 to 12g and in children daily doses of 150 to 200mg/kg divided in equal doses every 6 to 8 hours are recommended. For the new-born, 50mg/kg of cefotaxime can be given every 12h to infants 0-7 of age and every 8h to those 7-28 days of age. ***Intra-abdominal infections:*** Intraabdominal infection should be treated with Cefotaxime in combination with other appropriate antibiotics that are active against anaerobic bacteria.
Duration of therapy: The duration of therapy with Cefotaxime depends on the clinical condition of the patient and varies according to the course of the disease. Administration of Cefotaxime should be continued until symptoms have subsided or evidence of bacterial eradication has been obtained. Treatment over at least 10 days is necessary in infections caused by *Streptococcus pyogenes* (Parenteral therapy may be switched to an adequate oral therapy before the end of the 10 days period).
Dosage in renal functional impairment: In adult patients with a creatinine clearance of ≤ 5ml/min, the initial dose is similar to the recommended usual dose but the maintenance dose should be halved without change in the frequency of dosing.
Dosage in dialysis or peritoneal dialysis: In patients on haemodialysis and peritoneal dialysis an IV injection of 0.5g- 2g, given at the end of each dialysis session and repeated every 24 hours, is sufficient to treat most infections efficaciously.
Method of administration:
In order to prevent any risk of infection, the preparation of the infusion should be done in close aseptic conditions. Do not delay the infusion after the preparation of the solution. Cefotaxime and aminoglycosides should not be mixed in the same syringe or perfusion fluid.

- **Intravenous infusion:** For short intravenous infusion 1g or 2g Cefotaxime should be dissolved in 40-50ml Water for Injections or in another compatible fluid (e.g. glucose 10%). After preparation the solution should be given as a 20 minute intravenous infusion. For long lasting intravenous infusion 2g Cefotaxime should be dissolved in 100ml of a suitable fluid e.g. 0.9 % sodium chloride or isotonic glucose solution or other compatible fluids for infusions. After preparation, the solution may be given as a 50- 60 minute intravenous infusion.
- **Intravenous injection:** For intravenous injection Cefotaxime 0.5g should be dissolved in 2ml Water for Injections, Cefotaxime 1g should be dissolved in 4ml Water for Injections, Cefotaxime 2g should dissolved in 10 ml Water for Injections and should be injected over a period of 3-5 minutes. During post-marketing surveillance, potentially lifethreatening arrhythmia has been reported in a very few patients who received rapid intravenous administration of cefotaxime through a central venous catheter.
- **Intramuscular injection:** Cefotaxime 0.5g is dissolved in the 2ml Water for Injections or Cefotaxime 1g is dissolved in the 4ml Water for Injections. The solution should be administered by deep intramuscular injection. In order to prevent pain from injection Cefotaxime 0.5g may be dissolved in the 2ml 1% Lidocaine hydrochloride or Cefotaxime 1g may be dissolved in the 4ml 1% Lidocaine hydrochloride (only for adults). Solutions with lidocaine must not be administered intravenously. If the total daily dose is more than 2g, the intravenous administration should be chosen. In the case of severe infections, intramuscular injection is not recommended. The product information of the chosen lidocain-containing medicinal product must be regarded.

4.3. CONTRAINDICATIONS:

- Hypersensitivity, to the active substance cefotaxime or to any of the excipients.
- Hypersensitivity to cephalosporins.
- Previous immediate and/or severe hypersensitivity reaction to a penicillin or to any other type of beta-lactam drug.

4.4. SPECIAL WARNINGS AND PRECAUTIONS FOR USE:

As with other broad-spectrum antibiotics, prolonged use may result in the overgrowth of non-susceptible organisms. Repeated evaluation of the patient's condition is essential. If super-infection occurs during treatment, specific anti-microbial therapy should be instituted if considered clinically necessary.

- **Anaphylactic reactions:** As with all beta-lactam antibacterial agents, serious and occasionally fatal hypersensitivity reactions have been reported. In case of severe hypersensitivity reactions, treatment with cefotaxime must be discontinued immediately and adequate emergency measures must be initiated. Before beginning treatment, it should be established whether the patient has a history of severe hypersensitivity reactions to cefotaxime, to other cephalosporins or to any other type of beta-lactam agent. Caution should be used if cefotaxime is given to patients with a history of non-severe hypersensitivity to other beta-lactam agents.
- **Serious bullous reactions:** Cases of serious bullous skin reactions like Stevens-Johnson syndrome or toxic epidermal necrolysis have been reported with cefotaxime. Patients should be advised to contact their doctor immediately prior to continuing treatment if skin and/or mucosal reactions occur.
- ***Clostridium difficile* associated disease (e.g. pseudomembranous colitis):** Diarrhoea, particularly if severe and/or persistent, occurring during treatment or in the initial weeks following treatment, may be symptomatic of *Clostridium difficile* associated disease (CDAD). CDAD may range in severity from mild to life threatening, the most severe form of which is pseudomembranous colitis. The diagnosis of this rare but possibly fatal condition can be confirmed by endoscopy and/or histology. It is important to consider this diagnosis in patients who present with diarrhoea during or subsequent to the administration of cefotaxime. If a diagnosis of pseudomembranous colitis is suspected, cefotaxime should be stopped immediately and appropriate specific antibiotic therapy should be started without delay. *Clostridium difficile* associated disease can be favoured by faecal stasis. Medicinal products that inhibit peristalsis should not be given.

- **Haematological reactions:** Since Leukopenia, neutropenia and, more rarely, agranulocytosis may develop during treatment with cefotaxime, blood count should be monitored if treatment lasts for longer than 7 days. In case of neutropenia (< 1400 neutrophils/mm³), treatment should be stopped. Some cases of oeosinophilia and thrombocytopenia, rapidly reversible on stropping treatment, have been reported. Cases of haemolytic anemia have also been reported.
- **Patients with renal insufficiency:** The dosage should be modified according to the creatinine clearance calculated. Caution should be exercised if cefotaxime is administered together with aminoglycosides; probenecid or other nephrotoxic drugs. Renal function must be monitored in these patients, the elderly, and those with pre-existing renal impairment.
- **Neurotoxicity:** High doses of beta-lactam antibiotics, including cefotaxime, particularly in patients with renal insufficiency, may result in encephalopathy (e.g. impairment of consciousness, abnormal movements and convulsions).
- **Precautions for administration:** During post-marketing surveillance, potentially life-threatening arrhythmia has been reported in a very few patients who received rapid intravenous administration of cefotaxime through a central venous catheter. The recommended time for injection or infusion should be followed.
- **Effects on laboratory tests:** As with other cephalosporins a positive Coombs test has been found in some patients treated with cefotaxime. This phenomenon can interfere with the cross-matching of blood. Urinary glucose testing with non-specific reducing agents may yield false-positive results. This phenomenon is not seen when a glucose-oxidase specific method is used.
- **Sodium:** Cefotaxime sodium 250mg, 500mg and 1g contains 12.62mg, 25.25mg and 50.5mg of sodium equivalent to 0.63%, 1.26% and 2.52% respectively, of the WHO recommended maximum daily intake of 2g sodium for an adult.

4.5. INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION:
Uricosurics: Probenecid interferes with the renal tubular transfer of cefotaxime, thereby increasing cefotaxime exposure about 2-fold and reducing renal clearance to about half at therapeutic doses. Due to the large therapeutic index of cefotaxime, no dosage adjustment is needed in patients with normal renal function. Dosage adjustment may be needed in patients with renal impairment.
Aminoglycoside antibiotics and diuretics: As with other cephalosporins, cefotaxime may potentiate the nephrotoxic effects of nephrotoxic drugs such as aminoglycosides or potent diuretics (e.g. furosemide). Renal function must be monitored in these patients.
Certain antibiotics: Tetracyclines (such as doxycycline or minocycline), erythromycin, chloramphenicol. They may not work properly if used with Cefotaxime.

4.6. FERTILITY, PREGNANCY AND LACTATION:
Pregnancy: The safety of cefotaxime has not been established in human pregnancy. Cefotaxime crosses the placental barrier. Therefore, cefotaxime should not be used during pregnancy unless the anticipated benefit outweighs any potential risks.
Breast-feeding: Cefotaxime is excreted into human breast milk. Effects on the physiological intestinal flora of the breast-fed infant leading to diarrhoea, colonisation by yeast-like fungi, and sensitization of the infant cannot be excluded. Therefore, a decision must be made whether to discontinue breast-feeding or to discontinue therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

4.7. EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:
There is no evidence that cefotaxime directly impairs the ability to drive or to operate machines. High doses of cefotaxime, particularly in patients with renal insufficiency, may cause encephalopathy (e.g. impairment of consciousness, abnormal movements and convulsions). Patients should be advised not to drive or operate machinery if any such symptoms occur.

4.8. UNDESIRABLE EFFECTS:
Very Common (≥ 1/10), Common (≥ 1/100 to < 1/10), Uncommon (≥ 1/1,000 to <1/100), Rare (≥ 1/10,000 to 1/1,000), Very rare (< /10,000), Not known (cannot be estimated from available data).
- **Infections and infestations:** ***Not Known:*** Superinfection.
- **Blood and lymphatic system disorders:** ***Uncommon:*** Leukopenia, oeosinophilia, thrombocytopenia. ***Not Known:*** Neutropenia, agranulocytosis, haemolytic anaemia.
- **Immune system disorders:** ***Uncommon:*** Jarisch Herxheimer reaction. ***Not known:*** Anaphylactic reactions, angioedema, bronchospasm, anaphylactic shock.
- **Nervous system disorders:** ***Uncommon:*** Convulsions. ***Not known:*** Headache, dizziness, encephalopathy (e.g. impairment of consciousness, abnormal movements).
- **Cardiac disorders:** ***Not Known:*** Arrhythmia following rapid bolus infusion through central venous catheter.
- **Gastrointestinal disorders:** ***Uncommon:*** Diarrhoea. ***Not Known:*** Nausea, vomiting, abdominal pain, pseudomembranous colitis.
- **Hepatobiliary disorders:** ***Uncommon:*** Increase in liver enzymes (ALAT, ASAT, LDH, gamma-GT and/or alkaline phosphatase) and/or bilirubin. ***Not Known:*** Hepatitis (sometimes with jaundice).
- **Skin and subcutaneous tissue disorders:** ***Uncommon:*** Rash, pruritus, urticaria. ***Not known:*** Erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis.
- **Renal and urinary disorders:** ***Uncommon:*** Decrease in renal function/increase of creatinine (particularly when coprescribed with aminoglycosides). ***Not Known:*** Interstitial nephritis
- **General disorders and administration site conditions:** ***Very common:*** For IM formulations: Pain at the injection site, ***Uncommon:*** Fever, inflammatory reactions at the injection site, including phlebitis/ thrombophlebitis. ***Not known:*** For IM formulations (since the solvent contains lidocaine): systemic reactions to lidocaine.

4.9. OVERDOSE:
Symptoms of overdose may largely correspond to the profile of side effects. There is a risk of reversible encephalopathy in cases of administration of high doses of β-lactam antibiotics including cefotaxime. In case of overdose, cefotaxime must be discontinued, and supportive treatment initiated, which includes measures to accelerate elimination, and symptomatic treatment of adverse reactions (e.g. convulsions). No specific antidote exists. Serum levels of cefotaxime can be reduced by haemodialysis or peritoneal dialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1. PHARMACODYNAMIC PROPERTIES:
Pharmacotherapeutic group: Third-generation cephalosporins. **ATC code:** J01DD01
Mechanism of action: The bactericidal activity of cefotaxime results from the inhibition of bacterial cell wall synthesis (during the period of growth) caused by an inhibition of penicillin-binding proteins (PBPs) like transpeptidases.
Mechanism of resistance: A resistance to cefotaxime may be caused by following mechanisms:
- Inactivation by β-lactamases. Cefotaxime can be hydrolysed by certain β-lactamases, especially by extended-spectrum β-lactamases (ESBLs) which can be found in strains of *Escherichia coli* or *Klebsiella pneumoniae*, or by chromosomal encoded inducible or constitutive β-lactamases of the AmpC type which can be detected in Enterobacter cloacae. Therefore, infections caused by pathogens with inducible, chromosomal encoded AmpC- β-lactamases should not be treated with cefotaxime even in case of proven in-vitro-susceptibility because of the risk of the selection of mutants with constitutive, derepressed AmpC- β-lactamases-expression.
- Reduced affinity of PBPs against cefotaxime. The acquired resistance of Pneumococci and other Streptococci is caused by modifications of already existing PBPs as a consequence of a mutation process. In contrast to this concerning the methicillin-(oxacillin-)resistant Staphylococcus, the creation of an additional PBP with reduced affinity against cefotaxime is responsible for resistance.
- Inadequate penetration of cefotaxime through the outer cell membrane of gram-negative bacteria so that the inhibition of the PBPs is insufficient.
- The presence of transport mechanism (efflux pumps) being able to actively transport cefotaxime out of the cell.

A complete cross resistance of cefotaxime occurs with ceftriaxone and partially with other penicillins and cephalosporins.
Breakpoints: The following minimal inhibitory concentrations were defined for sensitive and resistant germs: EUCAST (European Committee on Antimicrobial Susceptibility Testing) break points V3.1(2013-02-11):

Pathogen	Susceptible	Resistant
Enterobacteriaceae	≤ 1mg/l	> 2mg/l
Staphylococcus spp.	--*	--*
Streptococcus (group A, B, C, G)	--**	--**
Viridans group streptococci	≤ 0.5mg/l	> 0.5mg/l
Streptococcus pneumoniae	≤ 0.5mg/l***	> 2mg/l
Haemophilus influenzae	≤ 0.12mg/l***	> 0.12mg/l
Moraxella catarrhalis	≤ 1mg/l	> 2mg/l
Neisseria gonorrhoeae	≤ 0.12mg/l	> 0.12mg/l
Neisseria meningitidis	≤ 0.12mg/l***	> 0.12mg/l
Not species-specific breakpoints****	≤ 1mg/l	> 2mg/l

* Susceptibility of staphylococci to cephalosporins is inferred from the cefoxitin susceptibility except for ceftazidime, cefixime and ceftibuten, which do not have breakpoints and should not be used for staphylococcal infections. Some methicillin-resistant *S. aureus* are susceptible to ceftaroline. ** The beta-lactam susceptibility of streptococcus groups A, B, C and G is inferred from the penicillin susceptibility. *** Isolates with MIC values above the susceptible breakpoint are very rare or not yet reported. The identification and antimicrobial susceptibility tests on any such isolate must be repeated and if the result is confirmed the isolate sent to a reference laboratory. Until there is evidence regarding clinical response for confirmed isolates with MIC values above the current resistant breakpoint they should be reported resistant. **** Breakpoints apply to a daily intravenous dose of 1g x 3 and a high dose of at least 2g x 3.

Susceptibility: The prevalence of acquired resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections. If the efficacy of cefotaxime is questionable due to the local prevalence of resistance, expert opinion should be sought regarding the choice of therapy. In particular in the case of severe infections or failure of therapy a microbiological diagnosis including a verification of the germ and its susceptibility should be aspired.

SUMMARY OF PRODUCT CHARACTERISTICS

Commonly susceptible species: ***Gram-positive aerobes:*** *Staphylococcus aureus* (methicillin-susceptible), *Streptococcus agalactiae*, *Streptococcus pneumoniae* (incl. penicillin-resistant strains), *Streptococcus pyogenes*. ***Gram-negative aerobes:*** *Borrelia burgdorferi*, *Haemophilus influenzae*, *Moraxella catarrhalis*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Proteus mirabilis*, *Proteus vulgaris*.
Species for which acquired resistance may be a problem: ***Gram-positive aerobes:*** *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Staphylococcus hominis*. ***Gram-negative aerobes:*** *Citrobacter freundii*, *Enterobacter aerogenes*, *Enterobacter cloacae*, *Escherichia coli*, *Klebsiella oxytoca*, *Klebsiella pneumoniae*, *Morganella morganii*, *Serratia marcescens*. ***Anaerobes:*** *Bacteroides fragilis*.
Inherently resistant species: ***Gram-positive aerobes:*** *Enterococcus* spp., *Listeria monocytogenes*, *Staphylococcus aureus* (methicillin-resistant). ***Gram-negative aerobes:*** *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Stenotrophomonas maltophilia*. ***Anaerobes:*** *Clostridium difficile*. ***Others:*** *Chlamydia* spp., *Chlamydophila* spp., *Legionella pneumophila*, *Mycoplasma* spp., *Treponema pallidum*.

5.2. PHARMACOKINETIC PROPERTIES:
Absorption: Cefotaxime is for parenteral application. Mean peak concentrations 5 minutes after intravenous injection are about 81-102mg/l following a 1g dose of cefotaxime and about 167-214mg/l 8 minutes after a 2g dose. Intramuscular injection produces mean peak plasma concentrations of 20 mg/l within 30 minutes following a 1g dose.
Distribution: Cefotaxime gives good penetration into different compartments. Therapeutic drug levels exceeding the minimum inhibitory levels for common pathogens can rapidly be achieved. Cerebrospinal fluid concentrations are low when the meninges are not inflamed but cefotaxime usually passes the blood-brain barrier in levels above the MIC of the sensitive pathogens when the meninges are inflamed (3-30µg/ml). Cefotaxime concentrations (0.2-5.4µg/ml), inhibitory for most Gram-negative bacteria, are attained in purulent sputum, bronchial secretions and pleural fluid after doses of 1 or 2g. Concentrations likely to be effective against most sensitive organisms are similarly attained in female reproductive organs, otitis media effusions, prostatic tissue, interstitial fluid, peritoneal fluid and gall bladder wall, after therapeutic doses. High concentrations of cefotaxime and O-desacetylcefotaxime are attained in bile. Cefotaxime passes the placenta and attains high concentrations in foetal fluid and tissues (up to 6mg/kg). Small amounts of cefotaxime diffuse into the breast milk. Protein binding for cefotaxime is approximately 25-40%. The apparent distribution volume for cefotaxime is 21-37 l after 1g intravenous infusion over 30 minutes.
Biotransformation: Cefotaxime is partly metabolized in human beings. Approximately 15-25% of a parenteral dose are metabolized to the O-desacetylcefotaxime metabolite, which also has antibiotic properties.
Elimination: The main route of excretion of cefotaxime and O-desacetylcefotaxime is the kidney. Only a small amount (2%) of cefotaxime is excreted in the bile. In the urine collected within 6 hours 40-60% of the administered dose of cefotaxime is recovered as unchanged cefotaxime and 20% is found as O-desacetylcefotaxime. After administration of radioactive labelled cefotaxime more than 80% can be recovered in the urine, 50-60% of this fraction is unchanged cefotaxime and the rest contains metabolites. The total clearance of cefotaxime is 240-390ml/min and the renal clearance is 130-150ml/min. The serum half-lives of cefotaxime and O-desacetylcefotaxime are normally about 50-80 and 90 minutes respectively. In elderly, the serum half-life of cefotaxime is 120-150min. In patients with impaired renal function (creatinine clearance 3-10ml/min) the serum half-life of cefotaxime can be increased to 2.5-3.6 hours. In neonates, the pharmacokinetics are influenced by gestation and chronological age, the half-life being prolonged in premature and low birth weight neonates of the same age.

5.3. PRECLINICAL SAFETY DATA:
Preclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, and toxicity to reproduction. Cefotaxime passes through the placenta. After intravenous administration of 1g Cefotaxime during the birth values of 14µg/ml were measured in the umbilical cord serum in the first 90 minutes after application, which dropped to approximately 2.5µg/ml by the end of the second hour after application. In the amniotic fluid, the highest concentration of 6.9µg/ml was measured after 3-4 hours. This value exceeds the MIC for most gram-negative bacteria.

6. PHARMACEUTICAL PARTICULARS

6.1. LIST OF EXCIPIENTS:
None

6.2. INCOMPATIBILITIES:
Cefotaxime should not be added with other antibiotics, in the same syringe or solution for infusion. This concerns especially aminoglycosides. Cefotaxime should not be mixed with solutions containing sodium bicarbonate. Cefotaxime is compatible with several commonly used intravenous infusion fluids:
- Water for Injection
- 0.9% Sodium Chloride solution
- 5% Glucose solution
- 5% Glucose/0.9% Sodium Chloride solution
- Ringer-lactate solution
- 5% Metronidazole solution
- Dextran 40 in 0.9% Sodium Chloride solution
- Dextran 40 in 5% Glucose solution

The compatibility of cefotaxime in other infusion fluids should be checked before use.

6.3. SHELF LIFE:
Unopened vial: See expiry on the pack.
Reconstituted solution:
For Intramuscular Injection: Cefotaxime sterile powder after reconstitution in water for injection or lidocaine hydrochloride injection solution 0.5% or 1% respectively is chemically stable:
- Up to 8 hours at room temperature (not exceeding + 25°C/indoor light).
- Up to 24 hours under refrigerated conditions (+2°C to 8°C/protected from light).

For Injection or Infusion in Water for Injection: Cefotaxime sterile powder after reconstitution in water for injection is chemically stable:
- Up to 12 hours at room temperature (not exceeding + 25°C/indoor light).
- Up to 24 hours under refrigerated conditions (+2°C to 8°C/protected from light).

A pale yellow color of the solution does not indicate impairment of the antibiotic activity.

6.4. SPECIAL PRECAUTIONS FOR STORAGE:
Do not store over 30°C, and protect from heat, light and moisture. Improper storage may deteriorate the medicine. Keep out of reach of children.
Freshly reconstituted solution is recommended.

6.5. NATURE AND CONTENTS OF CONTAINER:
Yorker® **250mg Injection:** ***Powder for Injection:*** Clear glass vial (USP Type-III) with bromobutyl rubber stopper, sealed with flip off seal. ***Water for Injection:*** Clear 2ml glass ampoule (USP Type-I). Pack size is 1 vial and 1 ampoule.
Yorker® **500mg Injection:** ***Powder for Injection:*** Clear glass vial (USP Type-III) with bromobutyl rubber stopper, sealed with flip off seal. ***Water for Injection:*** Clear 2ml glass ampoule (USP Type-I). Pack size is 1 vial and 1 ampoule
Yorker® **1g Injection:** ***Powder for Injection:*** Clear glass vial (USP Type-III) with bromobutyl rubber stopper, sealed with flip off seal. ***Water for Injection:*** Clear 4ml glass ampoule (USP Type-I). Pack size is 1 vial and 1 ampoule

6.6. SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING:
Aseptic techniques should be used to reconstitute the solution. The reconstituted solution should be administered immediately. Do not use if any particulate matter is visible. Withdraw only one dose. For single use only, discard unused portion. Any unused solution should be discarded. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

6.7. DRUG PRODUCT SPECIFICATION:
USP Specs.

7. MARKETING AUTHORISATION HOLDER

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

8. MARKETING AUTHORISATION NUMBER(S)

Yorker® **250mg Injection:** 047004
Yorker® **500mg Injection:** 047005
Yorker® **1g Injection:** 047006

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Yorker® **250mg Injection:** 04th September, 2007
Yorker® **500mg Injection:** 04th September, 2007
Yorker® **1g Injection:** 04th September, 2007

10. DATE OF REVISION OF THE TEXT

یورکر® انجکشن

(سیفٹوٹیکزائم سوڈیم)

برائے عضلاتی / وریدی استعمال

ہدایات:

خوراک ڈاکٹر کی ہدایت کے مطابق استعمال کریں

صرف رجسٹرڈ ڈاکٹر کے نسخے کے مطابق فروخت کریں

صرف ایک مرتبہ استعمال کے لئے ہے غیر استعمال شدہ دوا کو ضائع کردیں

بچوں کی پہنچ سے دور رکھیں

دوا کو ۳۰ ڈگری سینٹی گریڈ سے زیادہ درجہ حرارت پر نہ رکھیں،

گرمی، روشنی اور نمی سے محفوظ رکھیں ورنہ دوا خراب ہو جائیگی