Module-1 Administrative Information And Prescribing Information

1.3 Botswana labelling and packaging

1.3.1 Botswana package insert:

Enclosed

The following adverse events and altered laboratory tests have been reported for cephalosporin-class antibiotics: Stevens-Johnson syndrome, erythema multiformae, toxic epidermal necrolysis, toxic nephropathy, aplastic anaemia, haemolytic anaemia, haemorrhage, and false positive tests for urinary glucose.

Special Precautions:
Antibiotics should be administered with caution to any patient who has demonstrated some form of allergy, particularly to drugs. If an allergic reaction to TEICO occurs, discontinue the drug and treat the patient appropriately. Serious immediate hypersensitivity reactions may require epinephrine and other supportive therapy.
Pseudomembranous colitis has been reported with virtually all broad-spectrum antibiotics including cefepime; therefore, it is important to consider this diagnosis in patients who develop diarrhoea in association with the use of antibiotics. Mild cases of colitis may respond to drug discontinuation alone; moderate to severe cases may require more elaborate management.
Use of TEICO may result in overgrowth of nonsusceptible organisms. Should superinfection occur during therapy, appropriate measures should be taken.

Renal Impairment
Renal function should be monitored carefully if drugs with nephrotoxic potential, such as aminoglycosides and potent diuretics, are administered with TEICO.

Geriatric Use
Of the more than 6,400 adults treated with TEICO in clinical studies, 35% were 65 years or older while 16% were 75 years or older.
In clinical studies, when geriatric patients received the usual recommended adult dose, clinical efficacy and safety were comparable to clinical efficacy and safety in non-geriatric adult patients unless the patients had renal insufficiency. There was a modest prolongation in elimination half-life and lower renal clearance values compared with those seen in younger people. Dosage adjustments are recommended if renal function is compromised (see Dosage And Directions For Use).
Cefepime 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 renal function should be monitored (see Warnings, Side Effects and Pharmacological Action). Serious adverse events, including reversible encephalopathy (disturbance of consciousness including confusion, hallucinations, stupor, and coma) myoclonus, seizures (including nonconvulsive status epilepticus), and/or renal failure have occurred in geriatric patients with renal insufficiency given the usual dose of cefepime (see warnings and side effects).

Interaction with other medicaments and other forms of interaction
TEICO exhibits physical or chemical incompatibility when admixed with vancomycin hydrochloride, gentamycin sulfate, netilmycin sulfate and aminophylline.
In patients treated with TEICO, false positive urinary tests for glucose may result when reducing agents are employed. False positives are not seen with glucose-oxidase methods.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT
Treatment should be symptomatic and supportive.
In case of severe overdosage, especially in patients with compromised renal function, haemodialysis will aid in the removal of cefepime from the body; peritoneal dialysis is of no value. Accidental overdosing has occurred when large doses were given to patients with impaired renal function (see dosage and Administration, precautions and adverse reactions).

IDENTIFICATION
A white to pale yellow powder in a clear glass vial. When reconstituted, it is a clear colourless to pale yellow solution.

STORAGE INSTRUCTIONS
Dry Powder: Store at room temperature below 25°C and protect from light.
Keep out of reach of children

Manufactured by:
M. J. Biopharm Pvt. Ltd.
L-7, MIDC Indl, Area, Taloja.
Navi Mumbai 410 208 (INDIA)

TEICO - 500 (CEFEPIME FOR INJECTION USP 500 MG)
TEICO -1000 (CEFEPIME FOR INJECTION USP 1000 MG)

COMPOSITION
TEICO is a cephalosporin antibiotic intended for intramuscular or intravenous administration.
A **TEICO** vial contains Cefepime as active in the form of a sterile mix of Cefepime hydrochloride monohydrate and L-arginine. The L-arginine, at an approximate concentration of 725 mg/g of Cefepime, is added to control the pH of the constituted solution at 4,0 - 6,0.

PHARMACOLOGICAL CLASSIFICATION
Broad and Medium Spectrum Antibiotics.

PHARMACOLOGICAL ACTION
Microbiology
TEICO is a bactericidal agent that acts by inhibition of bacterial cell wall synthesis. Cefepime is a bactericidal agent that has a spectrum of activity against a range of Gram-positive and Gram-negative bacteria.

Cefepime is highly resistant to hydrolysis by a number of beta-lactamases, has a low affinity for chromosomally encoded beta-lactamases, and exhibits rapid penetration into Gram-negative bacterial cells.
Cefepime minimum bactericidal concentrations were ≤2 times the minimum inhibitory concentration for the majority of organisms tested.
Cefepime has been shown to be active against most strains tested of the following organisms both in vitro and in clinical infections.
Gram-positive aerobes:
Staphylococcus aureus (including penicillinase-producing strains but excluding methicillin-resistant staphylococci), *Streptococcus agalactiae* (Group B streptococci), *Streptococcus pneumoniae* (formerly Diplococcus pneumoniae), *Streptococcus pyogenes* (Group A streptococci), other beta-haemolytic streptococci (Groups C, G, F).

Gram-negative aerobes:
Acinetobacter calcoaceticus (subsp. *anitratus, lwoffi*), Enterobacter spp.(*including E. aerogenes, E. agglomerans, E. cloacae, E. sakazakii*), *Escherichia coli*, *Haemophilus influenzae*, (including strains of beta-lactamase producing *H. influenzae*), *Haemophilus parainfluenzae*, Klebsiella spp.(including *K. oxytoca, K. ozaenae, K. pneumoniae*), *Moraxella catarrhalis* (formerly *Branhamella catarrhalis*), *Morganella morganii, Proteus mirabilis, Pseudomonas aeruginosa* (not all strains), *Serratia marcescens*.
Cefepime exhibits *in vitro* minimum inhibitory concentrations (MIC's) of 8 mcg/mL or less against 90% or more of the strains of the following micro-organisms: however, *in vitro* activity does not necessarily imply clinical efficacy.
Gram-positive aerobes:
Note: Enterococci like *Enterococcus faecalis* and methicillin-resistant staphylococci, are resistant to Cefepime.
Staphylococcus aureus (including beta-lactamase-producing strains but excluding methicillin-resistant staphylococci), *Staphylococcus epidermidis* (including beta-lactamase-producing strains), *Staphylococcus hominis, Staphylococcus saprophyticus*, Group D streptococci (*Streptococcus bovis*), Viridans streptococci.
Gram-negative aerobes:
Pseudomonas putida, P. stutzeri, Proteus vulgaris, Aeromonas hydrophila, Capnocytophaga spp., Citrobacter spp. including *C. freundii, Campylobacter jejuni, Gardnerella vaginalis, Haemophilus ducreyi, Hafnia alvei, Neisseria gonorrhoeae* (including beta-lactamase-producing strains), *Neisseria meningitidis*, Providencia sp. including *P. rettgeri, P. stuartii,* Salmonella spp., *Serratia liquefaciens*, Shigella spp., *Yersinia enterocolitica*.

Anaerobes:
Clostridium perfringens, Mobiluncus spp.
Clinical Pharmacology
Adults
Following intramuscular injection, cefepime is completely absorbed. Therapeutic concentrations are found in various body fluids such as urine, bile, peritoneal fluid, blister fluid and sputum, and tissues such as bronchial mucosa, prostate, appendix and gallbladder, following intravenous administration of a single dose of cefepime.
The average elimination half-life of cefepime is approximately two hours.
There is no evidence of accumulation in healthy subjects receiving doses up to 2 g intravenously every 8 hours for a period of 9 days. Total body clearance averages 120 mL/min.
The average renal clearance of cefepime is 110 mL/min, demonstrating that cefepime is eliminated almost exclusively by renal mechanisms, primarily glomerular filtration.
Urinary recovery of unchanged cefepime represents approximately 85% of dose, resulting in high concentrations of cefepime in the urine.
The serum protein binding of cefepime averages 16,4% and is independent of concentration in the serum.
Healthy volunteers 65 years old or older, who received a single 1g intravenous dose of cefepime had higher area under the concentration-time curve and lower renal clearance values compared to younger healthy adults. Dosage adjustments in the elderly are recommended if renal function is compromised (see warnings and dosage and administration).
The pharmacokinetics of cefepime were unaltered in patients with impaired hepatic function who received a single 1g dose.
Elimination half-life is prolonged in patients with various degrees of renal insufficiency with a linear relationship between total body clearance and creatinine clearance. This serves as the basis for dosage adjustment recommendations in this group of patients (see Dosage And Directions For Use).
Average half-life in severely impaired patients requiring dialysis therapy is 13 hours for haemodialysis and 19 hours for continuous ambulatory peritoneal dialysis.
Paediatrics
Single and multiple-dose pharmacokinetics of cefepime were evaluated in patients ranging in age from 2 months to 16 years who received 50 mg/kg doses administered by IV infusion or IM injection: multiple doses were administered every 8 or 12 hours for at least 48 hours.
Mean plasma concentrations of cefepime after the first dose were similar to those at steady state, with only slight accumulation seen upon repeated dosing.
Following IM injection under steady state conditions, mean peak cefepime plasma concentrations of 68 mcg/mL were achieved at a median time of 0,75 hours, compared to 185,6 mcg/mL after IV. The mean trough concentration after IM injection at steady state was 6,0 mcg/mL at 8 hours. Bioavailability averaged 82% after IM injection.
Other pharmacokinetic parameters in infants and children were not different between first-dose and steady-state determinations, regardless of dosing schedule (q12h or q8h). There were also no differences in pharmacokinetics among various patient ages or between males and female patients.
Following a single IV dose, total body clearance (in children over 6 months) averaged 3,4 mL/min/kg and average volume of distribution was 0,3 L/kg. The overall mean elimination half-life was 1,6 hours. The urinary recovery of unchanged cefepime was 60,4% of the administered dose, and renal clearance was the primary pathway of elimination, averaging 2,0 mL/min/kg. Elimination was slower in children 2 - 6 months (t½1,89 hours, clearance 2,97 mL/min/kg).

Concentrations of cefepime in cerebrospinal fluid relative to those in plasma are shown in Table 1.
TABLE 1
Mean (SD) Plasma (PL) and CSF Concentrations, and CSF/PL Ratios of Cefepime in Infants and Children*

Sampling Time (hr)	N	Plasma concentration (mcg/mL)	CSF concentration (mcg/mL)	Ratio CSF/PL
0,5	6	70,4 (55,4)	5,7 (8)	0,12 (0,14)
1	4	44,1 (7,8)	4,3 (1,5)	0,10 (0,04)
2	5	23,9 (12,9)	3,6 (2,0)	0,17 (0,09)
4	5	11,7 (15,7)	4,2 (1,1)	0,87 (0,56)
8	5	4,9 (5,9)	3,3 (2,8)	1,02 (0,64)

* Patients ranged in ages from 3,1 months to 14,7 years, with a mean (SD) age of 2,9 (3,9) years. Patients with suspected central nervous system infection were treated with cefepime at a dose of 50 mg/kg administered as an IV infusion over 5 to 20 minutes every 8 hours. Single plasma and CSF samples were collected from selected patients at the sampling times shown relative to the end of infusion on day 2 or 3 of cefepime treatment

INDICATIONS
Adults
TEICO is indicated in the treatment of the infections listed below when caused by susceptible bacteria. Culture and susceptibility studies should be performed to determine susceptibility of the causative organism(s) to cefepime.

LOWER RESPIRATORY TRACT INFECTIONS:
Nosocomial and Community-Acquired Pneumonia caused by *Staphylococcus aureus* (methicillin-susceptible strains), *Pseudomonas aeruginosa*, Klebsiella species (including *Klebsiella pneumoniae*), Enterobacter species, *Escherichia coli*, *Proteus mirabilis*, *Streptococcus pneumoniae* (including intermediate penicillin resistant strains), *Haemophilus influenzae* (including beta-lactamase producing strains), *Haemophilus parainfluenzae* and *Moraxella (Branhamella) catarrhalis* (including beta-lactamase producing strains), including cases associated with **Bacteremia**. When *P. aeruginosa* is isolated or suspected, combination therapy with an aminoglycoside should be used.
Acute Bacterial Exacerbation of Chronic Bronchitis and Acute Bronchitis due to *Streptococcus pneumoniae* (including intermediate penicillin resistant strains), *Haemophilus influenzae* (including beta-lactamase producing strains), *Moraxella (Branhamella) catarrhalis* (including beta-lactamase producing strains).

URINARY TRACT INFECTIONS:
Complicated Urinary Tract Infections caused by *Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumoniae, Proteus mirabilis* and Enterobacter species, including cases associated with **Bacteremia**. When *P. aeruginosa* is isolated or suspected, combination therapy with an aminoglycoside should be used.
Uncomplicated Urinary Tract Infections due to *Escherichia coli*, *Proteus mirabilis*, Klebsiella species and Enterobacter species.

SKIN AND SKIN STRUCTURE INFECTIONS:
Skin and Skin Structure Infections caused by *Staphylococcus aureus* (methicillin-susceptible strains), *Streptococcus pyogenes* (Group A streptococci), *Streptococcus agalactiae* (Group B streptococci), other beta-haemolytic Streptococcus species, Enterobacter species, Klebsiella species, *Proteus mirabilis*, *Morganella morganii, Escherichia coli, Serratia marcescens* and *Acinetobacter calcoaceticus.*

INTRA-ABDOMINAL INFECTIONS:
Complicated Intra-abdominal Infections Including Peritonitis and Biliary Tract Infections caused by *Escherichia coli*, sensitive *Pseudomonas aeruginosa*. Peritonitis is often polymicrobial and may include anaerobic micro-organisms such as Bacteroides species which are resistant to cefepime. When resistant anaerobes are suspected, cefepime should be combined with an antibiotic effective against these micro-organisms, including cases associated with **Bacteremia**.
In patients who are at risk of mixed aerobic-anaerobic infection, including infections in which *Bacteroides fragilis* may be present, concurrent therapy with an anti-anaerobic agent is recommended.

EMPIRIC TREATMENT IN FEBRILE NEUTROPENIA:
Cefepime is indicated for empiric monotherapy of febrile neutropenia. Combination of cefepime with other appropriate antimicrobial agents should be considered in patients at high risk for severe infection (including patients with a history of recent bone marrow transplantation, hypotension at presentation, an underlying haematologic malignancy, or severe or prolonged neutropenia) or when called for by host or local epidemiological factors.

Paediatrics
TEICO is indicated in paediatric patients (2 months and older) for the treatment of the infections listed below when caused by susceptible bacteria, (when *P. aeruginosa* is isolated or suspected, combination therapy with an aminoglycoside should be used):
LOWER RESPIRATORY TRACT INFECTION:
Pneumonia caused by *S. aureus, S. pneumoniae, H. influenzae.*

URINARY TRACT INFECTIONS:
Caused by *E. coli.*

SKIN AND SKIN STRUCTURE:
Infections caused by *Staphylococcus epidermidis*, streptococcus, *S. aureus, S. pyogenes.*

EMPIRIC TREATMENT IN FEBRILE NEUTROPENIA:
Cefepime is indicated for empiric monotherapy of febrile neutropenia. Combination of cefepime with other appropriate antimicrobial agents should be considered in patients at high risk for severe infection (including patients with a history of recent bone marrow transplantation, hypotension at presentation, an underlying haematologic malignancy, or severe or prolonged neutropenia) or when called for by host or local epidemiological factors.

CONTRAINDICATIONS
TEICO is contraindicated in patients who have had previous hypersensitivity reactions to any component of the formulation, the cephalosporin class of antibiotics, penicillins or other beta-lactam antibiotics.
Pregnancy and lactation:
Safety of use in pregnancy and lactation has not been established.
WARNINGS
In patients with impaired renal function, such as reduction of urinary output because of renal insufficiency (creatinine clearance ≤50 mL/min) or other conditions that may compromise renal function, the dosage of TEICO should be adjusted to compensate for the slower rate of renal elimination. Because high and prolonged serum antibiotic concentrations can occur from usual dosages in patients with renal insufficiency or other conditions that may compromise renal function, the maintenance dosage should be reduced when cefepime is administered to such patients. Continued dosage should be determined by degree of renal impairment, severity of infection, and susceptibility of the causative organisms (see dosage and directions for use and clinical pharmacology). During postmarketing surveillance, the following serious adverse events were reported: reversible encephalopathy (disturbance of consciousness including confusion, hallucinations, stupor, and coma), myoclonus, seizures (including nonconvulsive status epilepticus), and/or renal failure (see Side Effects). Most cases occurred in patients with renal impairment who received doses of TEICO that exceeded recommendations. In general, symptoms of neurotoxicity resolved after discontinuation of cefepime and/or after hemodialysis however, some cases included a fatal outcome.
DOSAGE AND DIRECTIONS FOR USE
TEICO can be administered either intravenously or intramuscularly.
The dosage and route vary according to the susceptibility of the causative organisms, the severity of the infection, and the overall condition and renal function of the patient.
Adults
Guidelines for dosage of TEICO for adults with normal renal function are provided in Table 2.

TABLE 2
Recommended dosage schedule for Adults with Normal Renal Function (aged 12 years and older)*

SITE AND TYPE OF INFECTION	DOSE		FREQUENCY
Mild to moderate urinary tract infections (uncomplicated and complicated)	500 mg - 1g IV or IM		q12h
Mild to moderate infections including bronchitis, skin and skin-structure infections	1g IV or IM		q12h
Severe infections including pneumonia, urinary tract infections, complicated intra-abdominal infections, including cases with an associated bacteremia	2g IV		q12h
Empiric treatment of fever in neutropenic patients	2g IV		q8h

* Usual duration of therapy is 7-10 days; more severe infections may require longer treatment. In the treatment of beta-haemolytic streptococcal infections a therapeutic dose must be administered for at least 10 days. For empirical treatment of Febrile neutropenia, usual duration of therapy is 7 days or until resolution of neutropenia.

Paediatrics (aged 1 month up to 12 years with normal renal function)
Usual Recommended dosages:
Pneumonia, urinary tract infections, and skin structure infections: Patients 2 months of age with body weight ≤40 kg: 50 mg/kg q12h for 10 days. For more severe infections, a dosage schedule of q8h can be used.
Empiric treatment of febrile neutropenia: Patients >2 months of age with body weight ≤40 kg: 50 mg/kg q8h for 7-10 days.
Experience with the use of TEICO in paediatric patients <2 months of age is limited. While this experience has been attained using the 50 mg/kg dose, modelling of pharmacokinetic data obtained in patients >2 months of age suggests that a dosage of 30 mg/kg q12h or q8h may be considered for patients aged 1 month up to 2 months.
Administration of TEICO in these patients should be carefully monitored.
For paediatric patients with body weights > 40 kg, adult dosing recommendations apply (see Table 2). For patients older than 12 years who are ≤40 kg, the dosage recommendations for younger patients ≤40 kg should be used. Dosage in paediatric patients should not exceed the maximum recommended dosage in adults (2g q8h). Experience with intramuscular administration in paediatric patients is limited.
Elderly
Dose adjustment is not required, unless there is concurrent renal impairment.
Impaired hepatic function
No adjustment is necessary for patients with impaired hepatic function.
Impaired renal function
The initial dose of Cefepime is the same as in patients with normal renal function. The recommended maintenance doses of cefepime in patients with renal insufficiency are presented in Table 3.
TABLE 3: Maintenance dosing schedule in adult patients with renal impairment *

Creatinine clearance (mL/min)	Recommended Maintenance Dosage			
> 50	Usual dose, no adjustment necessary			
	2g q8h	2g q12h	1g q12h	500 mg q12h
30 - 50	1g q8h	2g q24h	1g q24h	500 mg q24h
11 - 29	1g q 12h	1g q 24h	500 mg q 24h	500 mg q24h
≤10	1g q24h	500 mg q24h	250 mg q24h	250 mg q24h

*The initial dose is the same as in patients with normal renal function.
When only a serum creatinine measurement is available, the following formula may be used to estimate creatinine clearance. The serum creatinine should represent a steady state of renal function:

When only a serum creatinine measurement is available, the following formula may be used to estimate creatinine clearance. The serum creatinine should represent a steady state of renal function

Males:

$$\text{Creatinine clearance (mL/min)} = \frac{\text{Weight (kg)} \times (140 - \text{age})}{0{,}82 \times \text{serum creatinine (micromol/L)}}$$

Females:
0,85 x value calculated using the formula for males.

Dialysis Patients
In patients undergoing haemodialysis, approximately 68% of the total amount of cefepime present in the body at the start of dialysis will be removed during a 3 hour dialysis period.
A repeat dose, equivalent to the initial dose, should be given at the completion of each dialysis session. In patients undergoing continuous ambulatory peritoneal dialysis, cefepime may be administered at the same doses recommended for patients with normal renal function, i.e., 500 mg, 1g or 2g depending on infection severity, but at a dosage interval of every 48 hours.
Children with Impaired Renal Function
Since urinary excretion is the primary route of elimination of cefepime in paediatric patients (see Clinical Pharmacology), an adjustment of the dosage of TEICO should also be considered in patients <12 years of age with renal impairment.
Preparation of solution and Administration
TEICO powder is to be constituted using the volumes of diluent shown in Table 4; the diluents to be used are identified following this table.
TABLE 4: Preparations of solutions of TEICO

	Amount of diluent to be added (mL)	Approx. available volume (mL)	Approx. cefepime concentration (mg/mL)
Intravenous			
500 mg vial	5	5,7	90
1g vial	10	11,4	90
2g vial	10	12,8	160
Intra-muscular			
500 mg vial	1,5	2,2	230
1g vial	3,0	4,4	230

Intravenous (IV) administration: The IV route of administration is preferable for patients with severe or life-threatening infections, particularly if the possibility of shock is present.

For **direct** IV administration, constitute TEICO with Sterile Water for Injection, 5% Dextrose Injection or 0,9% Sodium Chloride, using the diluent volumes shown in Table 4. The resulting solution should be injected directly into the vein over a period of three to five minutes or injected into the tubing of an administration set while the patient is receiving a compatible IV fluid (see **Compatibility and Stability**).
For intravenous **infusion**, constitute the 500 mg, 1g, or 2g vial, as noted above for direct IV administration then, add the appropriate quantity of the resulting solution to an IV container with one of the compatible IV fluids identified under **Compatibility and Stability**. IV infusions of a volume between 50 mL and 100 mL should be administered over a period of approximately 30 minutes.
Intramuscular (IM) administration: TEICO should be constituted with one of the following diluents using the volumes shown in Table 4: Sterile Water for Injection, 0,9% Sodium Chloride Injection, 5% Dextrose Injection, or Bacteriostatic Water for Injection with Parabens or Benzyl Alcohol then administered by deep IM injection into a large muscle mass (such as the upper outer quadrant of the gluteus maximus). Although TEICO can be constituted with 0,5% or 1,0% Lidocaine hydrochloride, it is usually not necessary because TEICO causes little or no pain upon IM administration.
Compatibility and Stability
Intravenous: TEICO is compatible at concentrations between 1 and 40 mg/mL with one of the following IV infusion fluids: 0,9% Sodium Chloride Injection, 5% and 10% Dextrose Injection, M/6 Sodium Lactate Injection, 5% Dextrose and 0,9% Sodium Chloride Injection, Lactated Ringers and 5% Dextrose Injection. These solutions are stable for 24 hours at room temperature below 25°C or 7 days under refrigeration (2°C to 8°C) TEICO admixture compatibility and stability information is summarised in the following table:

TABLE 5: Cefepime admixture stability

TEICO concentration	Admixture and concentration	IV infusion solutions	Stability time for	
			RT/L (below 25°C)	Refrigeration (2°C to 8°C)
40 mg/mL	amikacin 6 mg/mL	NS or D5W	24 hours	7 days
4-40 mg/mL	clindamycin 0,25 –6 mg/mL	NS or D5W	24 hours	7 days
4 mg/mL	heparin 10-50 units/mL	NS or D5W	24 hours	7 days
4 mg/mL	potassium chloride 10-40 mEq/L	NS or D5W	24 hours	7 days
4 mg/mL	theophylline 0,8 mg/mL	D5W	24 hours	24 hours

NS =0,9% Sodium Chloride Injection
D5W =5% Dextrose Injection
RT/L =Room temperature and light

Solutions of TEICO, like those of most beta-lactam antibiotics, should not be added to solutions of metronidazole, vancomycin, gentamycin, tobramycin sulfate or netilmycin sulfate because of physical or chemical incompatibility. However, if concurrent therapy with TEICO is indicated, each of these antibiotics can be administered separately.
Intramuscular: TEICO constituted as directed (in Table 4) is stable for 24 hours at room temperature below 25°C or for 7 days under refrigeration (2°C to 8°C) when using the following diluents: Sterile Water for Injection, 0,9% Sodium Chloride, 5% Dextrose Injection, Bacteriostatic Water for Injection with Parabens or Benzyl Alcohol, or 0,5% or 1% Lidocaine hydrochloride.

NOTE: Parenteral drugs should be inspected visually for particulate matter before administration, and not used if particulate matter is present.
As with other cephalosporins, the colour of TEICO powder and solution may darken on storage, however, product potency is not adversely affected.

SIDE EFFECTS AND SPECIAL PRECAUTIONS
Side effects:
The most common side effects were gastrointestinal symptoms and sensitivity reactions. Adverse events that occurred are listed below by body system:

Hypersensitivity - anaphylaxis, rash, pruritus, urticaria, fever

Gastrointestinal - diarrhoea, nausea, vomiting, oral moniliasis, colitis (including pseudomembranous colitis), taste perversion, constipation, abdominal pain, dyspepsia

Cardiovascular vasodilation

Respiratory dyspnea

Central nervous system - headache, dizziness, paraesthesia, seizures have been reported
Other - fever, vaginitis, erythema, genital pruritus, chills and unspecified moniliasis. Hepatitis and cholestatic jaundice have occurred less frequently.
Local reactions such as phlebitis and inflammation at the site of IV injection and inflammation or pain at the site of intramuscular injection occurred with some patients.
Laboratory test abnormalities that developed in patients with normal baseline values during clinical trials were: elevations in alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, total bilirubin, eosinophilia, anaemia, thrombocytopenia and prolonged prothrombin time, partial thromboplastin time, and positive Coomb's test without haemolysis. Transient elevations of blood urea nitrogen, and/or serum creatinine and transient thrombocytopenia were observed. During postmarketing surveilance encephalopathy, disturbances of consiousness including confusion , hallucinations, stupor and coma, seizures, myoclonus, and/or renal failure have been reported in patients with renal impairment who received unadjusted doses of cefepime that exceeded recommendations in table 2 of Dosage and administration. (See also Precautions)
Anaphylaxis including anaphylactic shock, transient leukopenia, neutropenia, agranulocytosis and thrombocytopenia have been reported.
The safety profile of TEICO in infants and children is similar to that seen in adults. The most frequently-reported adverse event considered related to TEICO in clinical trials was rash.