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CEFTAZIDIME TEVA
POWDER FOR SOLUTION FOR INJECTION

Formulation and Strength
Ceftazidime Teva 1g or 2 g, sterile powder for solution for injection.

QUALITATIVE AND QUANTITATIVE COMPOSITION
Injection bottle containing ceftazidime pentahydrate, equivalent to 1 g and 2 g of ceftazidime.

Other Ingredients
Sodium carbonate (anhydrous) (E500).

PHARMACEUTICAL FORM
Ceftazidime Teva 1 g powder for solution for i.v./i.m. injection.
Ceftazidime Teva 2 g powder for solution for i.v. injection.

CLINICAL INFORMATION
Indications
Treatment of single or multiple infections caused by susceptible microorganisms.

In meningitis it is recommended that the results of a sensitivity test are known before treatment with ceftazidime as a single agent.

It may be used for infections caused by organisms resistant to other antibiotics including aminoglycosides and many cephalosporins.

When appropriate, however, it may be used in combination with an aminoglycoside or most other β-lactam antibiotics for example, in the presence of severe neutropenia, or with an antibiotic active against anaerobes when the presence of *Bacteroides fragilis* is suspected. In addition, ceftazidime is indicated in the perioperative prophylaxis of transurethral prostatectomy.

Indications include:
- severe infections in general
- respiratory tract infections including lung infections in cystic fibrosis
- ear, nose and throat infections
- urinary tract infections
- skin and soft tissue infections
- gastrointestinal, biliary and abdominal infections
- bone and joint infections
- Dialysis: infections associated with haemo- and peritoneal dialysis and with continuous ambulatory peritoneal dialysis (CAPD).

Dosage and Administration
Ceftazidime is to be used by the parenteral route, the dosage depending upon the severity, sensitivity, site and type of infection and the age, weight and renal function of the patient. Ceftazidime may be given intravenously or by deep intramuscular injection into a large muscle mass such as the upper outer quadrant of the gluteus maximus or lateral part of the thigh. Ceftazidime solutions may be given directly into the vein or introduced into the tubing of a giving set if the patient is receiving parenteral fluids.

Populations

Adults:

The adult dosage range for ceftazidime is 1 to 6 g per day 8 or 12 hourly (i.m. or i.v.).

In the majority of infections, 1 g 8-hourly or 2 g 12-hourly should be given.

In urinary tract infections, and in many less serious infections, 500 mg or 1 g 12-hourly is usually adequate.

In very severe infections, especially immunocompromised patients, including those with neutropenia, 2 g 8 or 12-hourly or 3 g 12-hourly should be administered.

When used as a prophylactic agent in prostatic surgery, 1 g (from the 1 g bottle) should be given at the induction of anaesthesia. A second dose should be considered at the time of catheter removal.

Elderly:

In view of the reduced clearance of ceftazidime in acutely ill elderly patients, the daily dosage should not normally exceed 3 g, especially in those over 80 years of age.

Cystic fibrosis:

In fibrocystic adults with normal renal function who have pseudomonal lung infections, high doses of 100 to 150 mg/kg/day as three divided doses should be used.

In adults with normal renal function 9 g/day has been used without ill effect.

Infants and children (greater than 2 months):

The usual dosage range for children aged over two months is 30 to 100 mg/kg/day, given as two or three divided doses.

Doses up to 150 mg/kg/day (maximum 6 g daily) in three divided doses may be given to infected immunocompromised or fibrocystic children or children with meningitis.

Neonates and children up to 2 months of age:

Whilst clinical experience is limited, a dose of 25 to 60 mg/kg/day given as two divided doses has proved to be effective. In the neonate the serum half-life of ceftazidime can be three to four times that in adults.

Renal impairment:

Ceftazidime is excreted by the kidneys. Therefore, in patients with impaired renal function it is recommended that the dosage of ceftazidime should be reduced to compensate for its slower excretion, except in mild impairment, i.e. glomerular filtration rate (GFR) greater than 50 ml/min. In patients with suspected renal insufficiency, an initial loading dose of 1 g of ceftazidime may be given. An estimate of GFR should be made to determine the appropriate maintenance dose.

Recommended maintenance doses are shown in the next column:

Recommended maintenance doses of ceftazidime in renal insufficiency			
Creatinine clearance ml/min	Approx. serum creatinine µmol/l (mg/dl)	Recommended unit dose of ceftazidime (g)	Frequency of dosing (hourly)
>50	<150(<1.7)	Normal dosage	
50-31	150-200 (1.7-2.3)	1	12
30-16	200-350 (2.3-4.0)	1	24
15-6	350-500 (4.0-5.6)	0.5	24
<5	>500 (>5.6)	0.5	48

* These values are guideline and may not accurately predict renal function in all patients especially in the elderly in whom the serum creatinine concentration may overestimate renal function.

In patients with severe infections, especially in neutropenics, who would normally receive 6 g of ceftazidime daily were it not for renal insufficiency, the unit dose given in the table above may be increased by 50% or the dosing frequency increased appropriately. In such patients it is recommended that ceftazidime serum levels should be monitored and trough levels should not exceed 40 mg/litre.

When only serum creatinine is available, the following formula (Cockcroft's equation) may be used to estimate creatinine clearance. The serum creatinine should represent a steady state of renal function:

Males:

$$\text{Creatinine clearance (ml/min)} = \frac{\text{weight (kg)} \times (140 - \text{age in years})}{72 \times \text{serum creatinine (mg/dl)}}$$

Females: 0.85 x above value.

To convert serum creatinine in µmol/litre into mg/dl divide by 88.4.

In children the creatinine clearance should be adjusted for body surface area or lean body mass and the dosing frequency reduced in cases of renal insufficiency as for adults.

Haemodialysis:

The serum half-life of ceftazidime during haemodialysis ranges from 3 to 5 hours. The appropriate maintenance dose of ceftazidime recommended in the above table should be repeated following each haemodialysis period.

Peritoneal dialysis:

Ceftazidime may also be used in peritoneal dialysis and continuous ambulatory peritoneal dialysis (CAPD).

As well as using ceftazidime intravenously, it can be incorporated into the dialysis fluid (usually 125 to 250 mg for 2 L of dialysis fluid).

For patients in renal failure on continuous arteriovenous haemodialysis or high-flux haemofiltration in intensive therapy units, it is recommended that the dosage should be 1 g daily either as a single dose or in divided doses. For low-flux haemofiltration it is recommended that the dosage should be that suggested under impaired renal function.

For patients on venovenous haemofiltration and venovenous haemodialysis, follow the dosage recommendations in the tables below:

Continuous venovenous haemofiltration dosage guidelines for ceftazidime

Residual renal function (creatinine clearance in ml/min)	**Maintenance dose (mg) for an ultrafiltration rate (ml/min) of [a]:**			
	5	16.7	33.3	50
0	250	250	500	500
5	250	250	500	500
10	250	500	500	750
15	250	500	500	750
20	500	500	500	750

[a] Maintenance dose to be administered every 12 h.

Ceftazidime dosage guidelines during continuous venovenous haemodialysis

Residual renal function (creatinine clearance in ml/min)	Maintenance dose (mg) for a dialysate in flow rate of [a]:					
	1.0 litre/h			2.0 litres/h		
	Ultrafiltration rate (litre/h)			Ultrafiltration rate (litres/h)		
	0.5	1.0	2.0	0.5	1.0	2.0
0	500	500	500	500	500	750
5	500	500	750	500	500	750
10	500	500	750	500	750	1000
15	500	750	750	750	750	1000
20	750	750	1000	750	750	1000

[a] Maintenance dose to be administered every 12 h.

Contraindications

Ceftazidime Teva is contra-indicated in patients with known hypersensitivity to cephalosporin antibiotics.

Hypersensitivity to ceftazidime pentahydrate or to any of the excipients of the injection.

History of severe hypersensitivity (e.g. anaphylactic reaction) to any other type of beta-lactam antibacterial agent (penicillins, monobactams and carbapenems).

Warnings and Precautions

Hypersensitivity 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 ceftazidime must be discontinued immediately and adequate emergency measures must be initiated.

As with other β-lactam antibiotics, before therapy with ceftazidime is instituted, careful inquiry should be made for a history of hypersensitivity reactions to ceftazidime, cephalosporins, penicillins or other drugs. Special care is indicated in patients who have experienced an allergic reaction to penicillin or other beta-lactams. CROSS-HYPERSENSITIVITY AMONG BETA-LACTAM ANTIBIOTICS HAS BEEN CLEARLY DOCUMENTED AND MAY OCCUR IN UP TO 10% OF PATIENTS WITH A HISTORY OF PENICILLIN ALLERGY. If an allergic reaction to ceftazidime occurs, discontinue the drug. Serious hypersensitivity reactions may require epinephrine (adrenaline), hydrocortisone, antihistamine or other emergency measures.

Ceftazidime has a limited spectrum of antibacterial activity. It is not suitable for use as a single agent for the treatment of some types of infections unless the pathogen is already documented and known to be susceptible or there is a very high suspicion that the most likely pathogen(s) would be suitable for treatment with ceftazidime. This particularly applies when considering the treatment of patients with bacteraemia and when treating bacterial meningitis, skin and soft tissue infections and bone and joint infections. In addition, ceftazidime is susceptible to hydrolysis by several of the extended spectrum beta lactamases (ESBLs). Therefore information on the prevalence of ESBL producing organisms should be taken into account when selecting ceftazidime for treatment.

Renal function

Cephalosporin antibiotics at high dosage should be given with caution to patients receiving concurrent treatment with high doses of cephalosporins and nephrotoxic drugs, e.g. aminoglycoside antibiotics, or potent diuretics such as frusemide, as these combinations are suspected of affecting renal function adversely. Clinical experience with ceftazidime has shown that this is not likely to be a problem at the recommended dose levels.

There is no evidence that ceftazidime adversely affects renal function at normal therapeutic doses: however, as for all antibiotics eliminated via the kidneys, it is necessary to reduce the dosage according to the degree of reduction in renal function to avoid the clinical consequences of elevated antibiotic levels, e.g. neurological sequelae, which have occasionally been reported when the dose has not been reduced appropriately (see Dosage and Administration in Renal Impairment).

Overgrowth of non-susceptible organisms

As with other broad spectrum antibiotics, prolonged use of ceftazidime may result in the overgrowth of non-susceptible organisms (e.g. Candida, Enterococci) which may require interruption of treatment or adoption of appropriate measures. Repeated evaluation of the patient's condition is essential.

As with other extended-spectrum cephalosporins and penicillins, some initially susceptible strains of *Enterobacter* spp., and *Serratia* spp. may develop resistance during ceftazidime therapy. When clinically appropriate during therapy of such infections, periodic susceptibility testing should be considered.

Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including ceftazidime, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of C. difficile.

C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of C. difficile cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

If CDAD is suspected or confirmed, ongoing antibiotic use not directed against C. difficile may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of C. difficile, and surgical evaluation should be instituted as clinically indicated.

Elevated levels of ceftazidime in patients with renal insufficiency can lead to seizures, encephalopathy, coma, asterixis, neuromuscular excitability, and myoclonia

Other Warnings

Cephalosporins may be associated with a fall in prothrombin activity. Those at risk include patients with renal and hepatic impairment, or poor nutritional state, as well as patients receiving a protracted course of antimicrobial therapy. Prothrombin time should be monitored in patients at risk and exogenous vitamin K administered as indicated.

Ceftazidime should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.

Distal necrosis can occur after inadvertent intra-arterial administration of ceftazidime.

Prescribing ceftazidime in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Interactions

Concurrent use of high doses with nephrotoxic drugs may adversely affect renal function (see Warnings and Precautions).

Ceftazidime does not interfere with enzyme-based tests for glycosuria. Slight interference with copper reduction methods (Benedict's, Fehling's, Clinitest) may be observed. Ceftazidime does not interfere in the alkaline picrate assay for creatinine.

The development of a positive Coombs' test associated with the use of ceftazidime in about 5% of patients may interfere with the cross-matching of blood. Chloramphenicol is antagonistic *in vitro* with ceftazidime and other cephalosporins. The clinical relevance of this finding is unknown, but if concurrent administration of ceftazidime with chloramphenicol is proposed, the possibility of antagonism should be considered.

Chloramphenicol has been shown to be antagonistic to beta-lactam antibiotics, including ceftazidime, based on in vitro studies and time kill curves with enteric gram-negative bacilli. Due to the possibility of antagonism in vivo, particularly when bactericidal activity is desired, this drug combination should be avoided.

In common with other antibiotics, ceftazidime may affect the gut flora, leading to lower oestrogen reabsorption and reduced efficacy of combined oral contraceptives. Therefore, alternative non-hormonal methods of contraception are recommended.

Pregnancy and Lactation

There is no experimental evidence of embryopathic or teratogenic effects attributable to ceftazidime but, as with all drugs, it should be administered with caution during the early months of pregnancy and in early infancy. Use in pregnancy requires that the anticipated benefit be weighed against the possible risks.

Ceftazidime is excreted in human milk in low concentrations and consequently caution should be exercised when ceftazidime is administered to a nursing mother.

Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. However, undesirable effects may occur (e.g. dizziness), which may influence the ability to drive and use machines

Information for patients

Patients should be counseled that antibacterial drugs, including ceftazidime, should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When ceftazidime is prescribed to treat a bacterial infection, patients should be told that although it is common to feel better early in the course of therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may: (1) decrease the effectiveness of the immediate treatment, and (2) increase the likelihood that bacteria will develop resistance and will not be treatable by ceftazidime or other antibacterial drugs in the future.

Diarrhea is a common problem caused by antibiotics which usually ends when the antibiotic is discontinued. Sometimes after starting treatment with antibiotics, patients can develop watery and bloody stools (with or without stomach cramps and fever) even as late as 2 or more months after having taken the last dose of the antibiotic. If this occurs, patients should contact their physician as soon as possible.

Adverse Reactions

Clinical trial experience has shown that ceftazidime is generally well tolerated.

Data from large clinical trials (internal and published) were used to determine the frequency of very common to uncommon undesirable effects. The frequencies assigned to all other undesirable effects were mainly determined using post-marketing data and refer to a reporting rate rather than a true frequency.

The following convention has been used for the classification of frequency:

very common $\geq$1/10
common $\geq$1/100 and <1/10
uncommon $\geq$1/1,000 and <1/100

rare ≥1/10,000 and <1/1,000
very rare <1/10,000.

Infections and infestations
Uncommon: Candidiasis (including vaginitis and oral thrush).

Blood and lymphatic system disorders
Common: Eosinophilia and thrombocytosis.
Uncommon: Leucopenia, neutropenia, and thrombocytopenia.
Very rare: Lymphocytosis, haemolytic anaemia, and agranulocytosis.

Immune system disorders
Very rare: Anaphylaxis (including bronchospasm and/or hypotension).

Nervous system disorders
Uncommon: Headache and dizziness.
Very rare: Paraesthesia.
There have been reports of neurological sequelae including tremor, myoclonia, convulsions, encephalopathy, and coma in patients with renal impairment in whom the dose of ceftazidime has not been appropriately reduced.

Vascular disorders
Common: Phlebitis or thrombophlebitis with i.v. administration.

Gastrointestinal disorders
Common: Diarrhoea.
Uncommon: Nausea, vomiting, abdominal pain, and colitis, antibacterial agent-associated diarrhoea and colitis
Very rare: Bad taste.
As with other cephalosporins, colitis may be associated with *Clostridium difficile* and may present as pseudomembranous colitis.

Renal and urinary disorders
Uncommon: Transient elevations of blood urea, blood urea nitrogen and/or serum creatinine
Very rare: Interstitial nephritis, acute renal failure.

Hepatobiliary disorders
Common: Transient elevations in one or more of the hepatic enzymes, ALT (SGPT), AST (SOGT), LDH, GGT and alkaline phosphate.
Very rare: Jaundice.

Skin and subcutaneous tissue disorders
Common: Maculopapular or urticarial rash.
Uncommon: Pruritus.
Very rare: Angioedema, erythemia multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis, DRESS (drug interaction with eosinophilia and systemic symptoms) *.
* There have been rare reports where DRESS has been associated with ceftazidime.

General disorders and administration site conditions
Common: Pain and/or inflammation after i.m. injection.
Uncommon: Fever.

Investigations

Common: Positive Coombs test.

Uncommon: As with some other cephalosporins, transient elevations of blood urea, blood urea nitrogen and/or serum creatinine have been observed.

A positive Coombs test develops in about 5% of patients and may interfere with blood cross-matching.

Postmarketing experience

The following events have been observed during clinical practice in patients treated with ceftazidime and were reported spontaneously. For some of these events, data are insufficient to allow an estimate of incidence or to establish causation.

General: Anaphylaxis; allergic reactions, which, in rare instances, were severe (e.g., cardiopulmonary arrest); urticaria; pain at injection site.

Hepatobiliary tract: Hyperbilirubinemia, jaundice.

Renal and genitourinary: Renal impairment.

Cephalosporin-Class Adverse Reactions: In addition to the adverse reactions listed above that have been observed in patients treated with ceftazidime, the following adverse reactions and altered laboratory tests have been reported for cephalosporin-class antibiotics:

Adverse Reactions: Colitis, toxic nephropathy, hepatic dysfunction including cholestasis, aplastic anemia, hemorrhage.

Altered Laboratory Tests: Prolonged prothrombin time, false-positive test for urinary glucose, pancytopenia.

Overdosage

Symptoms and Signs

Overdosage can lead to neurological sequelae including encephalopathy, convulsions and coma.

Symptoms of overdose can occur if the dose is not reduced appropriately in patients with renal impairment.

Treatment

Serum levels of ceftazidime can be reduced by haemodialysis or peritoneal dialysis.

CLINICAL PHARMACOLOGY

Pharmacodynamics

ATC classification

Pharmacotherapeutic group: cephalosporins ATC code: J01DD02

Ceftazidime is a bactericidal cephalosporin antibiotic which is resistant to most β-lactamases and is active against a wide range of gram-positive and gram-negative bacteria.

Pharmacokinetic Effects

Bacteriology

Ceftazidime is bactericidal in action, exerting its effect on target cell wall proteins and causing inhibition of cell wall synthesis. A wide range of pathogenic strains and isolates associated with hospital-acquired infections are susceptible to ceftazidime *in vitro*, including strains resistant to gentamicin and other aminoglycosides. It is highly stable to most clinically important β-lactamases produced by both gram-positive and gram-negative organisms and consequently is active against many ampicillin- and cephalothin-resistant strains.

Ceftazidime has high intrinsic activity *in vitro* and acts within a narrow MIC range for most genera with minimal changes in MIC at varied inoculum levels. *In vitro* the activities of ceftazidime and aminoglycosides in combination are additive. There is evidence of synergy in some strains.

Cefatizidime has been shown to have *in vitro* activity against the following organisms:

Gram-negative

Pseudomonas aeruginosa, Pseudomonas spp. (including *Ps. pseudomallei*), *Klebsiella pneumoniae, Klebsiella spp.(other),Proteus mirabilis, Proteus vulgaris, Morganella morganii* (formerly *Proteus morganii*), *Proteus rettgeri,* Providencia spp, *Escherichia coli,* Enterobacter spp, Citrobacter spp, Serratia spp, Salmonella spp, Shigella spp, Y*ersinia enterocolitica, Pasteurella multocida,* Acinetobacter spp, *Neisseria gonorrhoeae, Neisseria meningitides, Haemophilus influenzae* (including ampicillin-resistant strains), *Haemophilus parainfluenzae* (including ampicillin-resistant strains).

Gram-positive

Staphylococcus aureus (methicillin-sensitive strains), *Staphylococcus epidermidis* (methicillin-sensitive strains), Micrococcus spp, *Streptococcus pyogenes* (Group A beta-haemolytic streptococci), Streptococcus Group B (*S. agalactiae*),, *Streptococcus pneumoniae, Streptococcus mitis,* Streptococcus spp. (excluding *Enterococcus (Streptococcus) faecalis*).

Anaerobic strains

Peptococcus spp., Peptostreptococcus spp., Streptococcus spp, Propionibacterium spp., *Clostridium perfringens,* Fusobacterium spp., Bacteroides spp (many strains of *Bact. fragilis* are resistant).

Ceftazidime is not active *in vitro* against the following organisms: methicillin-resistant staphylococci, *Enterococcus (Streptococcus) faecalis* and many other Enterococci, *Listeria monocytogenes,* Campylobacter spp or *Clostridium difficile*.

In vitro the activities of ceftazidime and aminoglycoside antibiotics in combination have been shown to be at least additive; there is evidence of synergy in some strains tested. This property may be important in the treatment of febrile neutropenic patients.

Pharmacokinetics

Absorption

After intramuscular administration of 500 mg and 1 g, serum mean peak levels of 18 and 37 mg/litre respectively are rapidly achieved. Five minutes after an intravenous bolus of 500 mg, 1 g or 2 g, serum mean levels are respectively 46, 87 and 170 mg/l.

Distribution

Therapeutically effective concentrations are still found in the serum 8 to 12 hours after both intravenous and intramuscular administration. The serum half-life is about 1.8 hours in normal volunteers and 2.2 hours in patients with apparently normal renal function. The serum protein binding of ceftazidime is low at about 10%.

Concentrations of ceftazidime in excess of the mimimum inhibitory levels for common pathogens can be achieved in tissues such as bone, heart, bile, sputum, aqueous humour, synovial and pleural and peritoneal fluids. Transplacental transfer of the antibiotic readily occurs, and is excreted in the breast milk. Ceftazidime penetrates the intact blood brain barrier poorly and low levels are achieved in the CSF in the absence of inflammation. Therpeutic levels of 4 to 20 mg/litre or more are achieved in the CSF when the meninges are inflamed.

Metabolism

Ceftazidime is not metabolised in the body.

Elimination

Ceftazidime administered by the parenteral route reaches high and prolonged serum levels, which decrease with a half-life of about 2 h.

Ceftazidime is excreted unchanged in the active form into the urine by glomerular filtration. Approximately 80 to 90% of the dose is recovered in the urine within 24 hours. Less than 1% is excreted via the bile, significantly limiting the amount entering the bowel.

Special Patient Populations

Elimination of ceftazidime is decreased in patients with impaired renal function and the dose should be reduced (see Dosage and Administration - Renal impairment, Warnings and Precautions).

Preclinical safety data

No additional data of relevance.

PHARMACEUTICAL INFORMATION

Incompatibilities

Ceftazidime in sodium bicarbonate for injection is less stable than in other intravenous infusion liquids. Therefore this solution is not recommended for diluting Ceftazidime Teva.

If vancomycin is added to ceftazidime in solution sedimentation may occur. Therefore it deserves recommendation to flush the administration sets and the intravenous lines between the administration of both substances.

Ceftazidime and aminoglycosides must not be mixed with each other in the same infusion set or infusion syringe.

Shelf-life after reconstitution

The reconstituted product in water for injection or in the usual intravenous infusion fluids (see Instructions for use and handling) is physically-chemically stable for 8 hours at a temperature below 25°C or 24 hours in the refrigerator. From a microbiological standpoint however, the product should be used immediately after reconstitution. If the reconstituted product is not used immediately, the administrator is responsible for the handled term of use and the condition for administration.

Special precautions for storage of the unreconstituted injection bottle (vial)

Do not store above 25°C; store in the original container.
Protect from light.
Effervescence occurs on addition of water for injection.

Nature and contents of container

Injection bottles in 20 and 50 ml capacity (type I glass for 1 g, and type III for 2 g, with bromobutyl rubber stopper and aluminum flip-off cap) for Ceftazidime Teva 1000 mg and 2000 mg, respectively.

Instructions for use and handling

Compatibility with intravenous fluids

- Ceftazidime is compatible with the usual intravenous infusion fluids. Solutions with concentrations between 20 mg/ml and 40 mg/ml in the following infusion fluids may be stored to a maximum of 8 hours at temperatures at 25°C or 24 hours in the refrigerator.

Ceftazidime at concentrations between 1 mg/ml and 40 mg/ml is compatible with:
- physiological salt solution 0.9% g/v.
- sodium lactate solution 1/6 mol/L.
- formulated sodium lactate solutions (Hartmann's solution).
- glucose solution 5% g/v.
- sodium chloride 0.18% g/v plus glucose solution 4%.
- glucose solution 10% g/v.
- Dextran 40 solution 10% g/v in physiological salt solution 0.9% g/v.
- Dextran 40 solution 10% g/v in glucose solution 5% g/v.
- Dextran 70 solution 6% g/v in physiological salt solution 0.9% g/v.
- Dextran 70 solution 6% in glucose solution 5% g/v.

Ceftazidime in a concentration of 4 mg/ml for 8 hours at temperatures below 25°C or 24 hours in the refrigerator is compatible with:
- hydrocortisone (hydrocortisone sodium phosphate) 1 mg/ml in physiological salt solution 0.9% g/v or glucose solution 5% g/v.
- cefuroxime (cefuroxime sodium) 3 mg/ml in physiological salt solution 0.9% g/v.
- cloxacillin (cloxacillin sodium) 4 mg/ml in physiological salt solution 0.9% g/v.
- heparin 10 IE or 50 IE in physiological salt solution 0.9% g/v.
- potassium chloride solution 10 mmol/L or 40 mmol/L in physiological salt solution 0.9% g/v.

The contents of a bottle of Ceftazidime Teva may be mixed with metronidazole injection (500 mg in 100 ml) without loss of either efficacy. This solution has a maximum shelf life of 8 hours at temperatures below 25°C or 24 hours with storage in the refrigerator.

For intramuscular administration, Ceftazidime Teva may be mixed with a 0.5% or 1% lidocaine HCl for injection. The obtained solutions may be stored for 8 hours at temperatures below 25°C or 24 hours in the refrigerator.

Solutions with Ceftazidime Teva may vary in colour from light yellow to amber, dependent on the concentration, the type of diluent, and the conditions under which they are stored. Within the specified recommendations, the efficacy of the product is not negatively affected by such colour variations.

Instructions for reconstitution
In the table below are indicated the "to be added" volumes concentrations in the obtained solution, and the end volume of the obtained solution:

Vial size	**Amount of diluent to be added (ml)***	**Approximate concentration (mg/ml)**	**End volume (ml)**
1000 mg i.m..	3	260	3.9
1000 mg i.v.	10	90	10.9
1000 mg i.v. infusion	50 **	20	50.9
2000 mg i.v. bolus	10	170	11.8
2000 mg i.v. infusion	50**	40***	51.8

* For the diluent to be used see section "Compatibility with intravenous fluids"
** Adding in two phases.
*** Use Sodium Chloride Injection 0.9%. Dextrose Injection 5% or other approved diluent as Water for Injection produces hypotonic solutions at this concentration.

All bottles are closed under reduced pressure and delivered as such. When the contents dissolve, CO_2 is released and the pressure becomes positive. In order to make its use easier it is recommended to follow the reconstitution method below:

1. Stick the needle of the syringe through the stopper of the bottle and add the advised amount of diluent. The vacuum makes adding the diluent easier. Next pull out the needle.
2. Shake to dissolve the contents. CO_2 is released with this. In approximately 1-2 minutes a clear solution is obtained.
3. Invert the bottle. Stick the needle through the stopper of the bottle with the suction cap of the syringe completely pushed in. Draw the entire solution into the syringe (the pressure in the bottle makes withdrawal easier). Make sure the needle remains in the solution and does not project above the level of the liquid. The withdrawn solution may contain little CO_2 bubbles; this does not pose a problem.

Use of Ceftazidime Teva 2000 as a brief infusion

After reconstitution, the bottle of Ceftazidime Teva 2000 may serve as a brief intravenous infusion of 50 ml (for instance to a maximum of 30 minutes) as follows:

1. Stick the needle of the syringe through the stopper of the bottle and add 10 ml of diluent. The vacuum makes adding the diluent easier. Next pull out the needle.
2. Shake to dissolve the contents. CO_2 is released with this. In approximately 1-2 minutes a clear solution is obtained.
3. Stick an air venting cannula through the stopper of the bottle and add another 40 ml of diluent. Remove the air venting cannula and the needle of the syringe. Shake the bottle and set up for the infusion the usual way.

Note: To guarantee a sterile content of the bottle it is of importance not to put the air venting cannula through the stopper until after the preparation has dissolved.

REGISTRATION NUMBERS

Ceftazidime Teva 1 g: 143 79 31599 00.
Ceftazidime Teva 2 g: 143 78 31600 00.

MANUFACTURER

Vianex S.A.,
Greece.

For

Farmaprojects, S.A.,
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LICENCE HOLDER

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