EvoZid®

ایووزڈ

(Ceftazidime USP. 250,.500mg 8,..1gm)

For IM/IV Use

COMPOSITION
Evaid 250 mg:
Each vial of dry powder contains: CeftazidIme 250 mg as Ceftazidime pentahydrate USP

EvoZId 500 mg:
Each vial of dry powder contains: Ceftazidime 500 mg as Ceftazidime pentahydrate USP

EvoZId 1gm:
Each vial of dry powder contains: Ceftazidime lgm as Ceftazidime pentahydrate USP

PHARMACOKINETICS
Parenteral administration produces high and prolonged serum levels which decrease With a half-life of about 2 hours. After 1M administration of 500mg and 1g, peak levels of 18 and 37mg/I respectively are rapidly achieved, and 5 minutes after IV bolus Injection Of 500mg, 1g or 2g, serum levels :ire respectively 46, 87 and 170mg/I.

Therapeutically effective concentrations are still present in the serum 8-12 hours after either IV or IM administration.

Serum protein binding is about 10%.

Ceftazidime is not metabolised in the:body and is excreted unchanged, in active form into the urine by glomerular filtration; approximately 80-90% of the dose is recovered in the urine within 24 hours.

Eliminatien of Geftazidime is decreased in patients with inipaired renal function and the dose should be reduced.

Less than 1% is excreted via the bile, which limits the amount entering the bowel. Concentrations in excess of the MIC for common pathogens ciente achieved in tissues such as bone, heart, bile, sputum, aqueous humour, synovial, pleural and peritoneal fluids. Ceftazidime crosses the placenta readily, and is excreted in the breast milk. Penetration of the intact blood-brain barrier is poor resulting in low levels of ceftazkiime in the CSF in the absence of inflammation. However, therapeutic levels of 4•20m9/1 or more are achieved in the CSF When the Meninges are-fnftamect.

INDICATIONS
Treatment of single or multiple infections caused by susceptible.microorganierns. May be • used alone as first choice drug before the results of sensitivity testsiare available. May be used in combination with an aminoglycoside or most other betalactaun antibiotics. May be used with an antibiotic against anaerobes when the presence of Bacteroides.fragilis is suspected.

Indications Include:
- Severe infections e.g. septicaemia, bacteraemia, peritonitis, meningitis, Infections in immunosuppressed patients, infer/tons in patients in intensive care, e.g. infected bums. Respiratory tract infections including lung infections in cystic fibrosis.
- Ear, nose and throat infections.
- Urinary tract infections.
- Skin and soft tissue infections.
- Gastrointestinal, bifiary and abdominal infections.
- Bone and joint infections.
- Infections associated with haemo And peritoneal dialysis and with continuous ambulatory peritoneal dialysis (CAPD):
- Prophylaxis: Prostatic surgery (transurethral resection).

Bacteriology
Ceftazidime is bactericidal in action. it acts by inhibiting bacterial cell wall synthesis. A wide range of pathogenic strains and isolates are susceptible in vitro including strains resistant to gentamicin and other aminoglycosides. Ceftazidime is highly stable to most clinically important beta-lactamases produced by both Gram-positive &Gram-negative organisms, therefore it is active against many ampicillin and cephaiothin resistant strains.

Ceftazidime has high intrinsic activity in vitro and acts within a narrow MC 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.

Ceftazidime is active in vitro against the following organisms:
Gram-negative:

E. coil	Klebsiella app (including K. pneumoniae)
Proteus mirabilis	Proteus vulgaris
Morganella morganii	Proteus rettgeri
Pseudomonas spp (including P. aeruginosa)	Providenda spp
Enterobacter spp	Citrobacter spp
Serratia spp	Salmonella spp
Shigella spp	Yersinia enterocolitica
Pasteurella multocida	Acinetobacter spp
Neisseria gonorrhoeae	Neisseria meningitidis
Haemophilus infleenzae (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 (Strep. agalactiae)
iStreptococcus pneumoniae
Streptococcus mitis
Streptococcus see (excluding Enterococcus, Streptococcus faecalis)

Anaerdbic strains:

Peptococcus app	Peptostreptococcus spp
Streptococcus sop	Propionibacterium spp
Clostridium perfringens	Fusobacterium app

Bacteroides app (many strains of B: fragilis resistant)

Ceftazidime is not active in vitro against the following organisms:
Methicillin-resistant staphylococci .
'Streplococcus faecalis and many other Enterococci
Clostridium difficile.
Listeria monocytogenes
Campylobacter app

DOSAGE
Dosage depends upon the severity, Sensitivity, site and type of infection and upon the age and renal function of the patient.

Adults: 1-6g/day in 2 or 3 divided doses by iV or IM injection.

Urinary tract and less severe infections,	- 500mg or 1g every 12 hours.
Most infections	- lg every 8 hours or 2g every 12 hours
Very severe infections particularly in immunocompromised patients including those with neutropenia	- 2g every 8 or 12 hours .
Fibrocystic adults with pseudomonal lung infections	- 100-150mg/kg/day in 3 divided doses

When used as a prophylactic agent in prostatic surgery lg should be given at the induction of anaesthesia. A second dose should be considered at the time of catheter removal.

In adults with normal renal function 9g/day has been Used without ill effect. Infants and chitdren.(.2 months): 32.-100mg/kg/day in 2 or 3 divided doses. Doses opts, 150mg/ke/day (maximum 6g/day) in three divided doses may be given to infected immunocompromised or fibrocystic children or children with meningitis.

Neonates 10-2 months): 25-60mg/kgday in 2 divided doses. In neonates the serum half life of Geftazidime can be 3-4 times that in adults.
Use in the Elderly in view of the reduced clearance of ceftazidime in acutely ill elderly patients. the daily dosage should not normally exceed 3g, especially irrithose over 80 years of age.

Renal Impairment
Ceftazidime is excreted unchanged by the kidneys. Therefore in patients with impaired renal function the dosage should be reduced. An initial loading dose of 1g should be given.
Maintenance doses should be based on GFR:

Recommended maintenance doses of ceftazidime in renal insufficiency

Creatinine clearance (ml/min.)	Approx. Serum creatinine (mcmol/l) (mg/dl)	Recommended unit dose of ceftazidime (9)	Frequency of dosing (hourly)
>50	>150	-	normal dosage
50-31	150-200 (1.7-2.3)	1.0	12
30-16	200-350 (2.3-4.0)	1.0	24
15-6	350-500 (4.0-5.6)	0.5	24
<5	>500 (>5.6)	0.5	48

In patients with severe infections the unit dose should be increased by 50% or the dosing frequency increased. In such patients the ceftazidime serum levels should be monitored and trough levels should not exCeed 40mg/l.

In children the creatinine clearance should be adjusted 'for body surface area Of lean body mass.

Haemodialyals: The serum half-life during haemodialysis ranges from 3105 hours. Following each haemodialysis period the maintenance dose of ceftazidime recommended in the above table should be repeated.

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

In addition-to intravenous use, ceftazidime can be incorporated into the dialysis fluid (usually 125 to 250mg for 2 litres of dialysis solution). For patients in renal failure or continuous arteriovenous haemodialysis or high-flux haemofiltration in intensive therapy units; lg daily either as a single dose or in divided doses. For low-flux haemofiltration follow the dosage recommended under impaired renal function.

ADMINISTRATION
Use intravenously or by deep intramuscular injection. Recommended 1M injection sites are the upper outer quadrant of the gluteus maximus or lateral pan of the thigh.
Constitution Instructions: All sizes of vials are supplied under reduced pressure. As the product dissolves, carbon dioxide is released and a positive pressure develops. Small bubbles of carbon dioxide in the constituted solution may be ignored.

Vial Size	Route	Amount of Diluent to be added (ml)	Approximate Concentration (mg/ml)
250mg	intramuscular	1 ml	210
	intravenous	2.5ml	90
500mg	intramuscular	1.5ml	280
	intravenous	5ml	100
1g	intramuscular	3ml	280
	intravenous	10ml	100

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.

Ceftazidime is compatible with most commonly used intravenous fluids. Preparation of solutions for IM or IV bolus injection: •
1 . Introduce the syringe needle through the vial closure and inject the recommended volume of diluent.
2. Withdraw the needle and shake the vial to give a clear solution.
3. Invert the vial.. With the syringe piston fully depressed ensuring the needle into the solution. Withdraw the total volume of solution into the syringe ensuring that the needle remains in the solution. Small bubbles of carbon dioxide may be disregarded.

CONTRAINDICATIONS
Patients with known hypersensitivity to cephalosporin antibiotics.

WARNINGS
Before beginning treatment establish whether the patient has a history of hypersensitivity reactions to ceftazidime, cephalosporins, penicillins or other drugs.
Special caution is necessary when givitig Wtazidime to patients who have previouSly shown type I or immediate hypersensitivity reactions to penicillin.
If an allergic reaction to ceflazidime occurs discontinue the drug. Serious hypersensitivity reactions may require epinephrine (adrenaline), hydrocortisone, antihistamine or other emergency measures.

PRECAUTIONS
Concurrent treatment with high doses of cephalosporins and nephrotoxic drugs such as aminoglycosides or potent diuretics (e.g. frusemide) may adversely affect renal function. Clinical experience has shown that this is not likely to be a problem with ceftazidime at the recommended dose levels.

There is no evidence that ceftazidime adversely effects renal function at normal therapeutic doses.

Ceftazidime is eliminated via the kidneys, therefore the dosage should be reduced according to the degree of renal impairment. Neurological sequelae have occasionally been reported when the dose has not been reduced appropriately. (see Dosage in Impaired Renal Function). There is no experimental evidence of embryopathic or teratogenic effects, but as with all . drugs, ceftazidime should be administered with caution during the early months of pregnancy and early infancy. Ceftazidime is excreted in human milk in small quantities and should be used with caution in nursing mothers.

SIDE-EFFECTS
Ceftazidime is generally well tolerated. Adverse reactions are infrequent and includes;
Local: Phlebitis or thrombophlebitis with IV administration, pain and/or inflammation after ,JM injection.
Hypersensitivity: Maculopapular or urticarial rash, fever, pruritus, and very rarely angioedema and anaphylaxis (including bronchospasm and/or hypotension). As with other cephalosporins, there have been rare reports of toxic epidermal necrolysis.
Gastrointestinal: Diarrhoea, nausea, vomiting, abdominal pain, and very rarely oral thrush or colitis.
Genito-urinary: Candidiasis. vaginitis. .
Central Nervous System: Headache, dizziness, paraesthesia and bad taste.
Laboratory Test Changes: Transient changes noted during ceftazidime therapy include; eosinophilia, positive Coomb's tests, very rarely haemolytic anaemia, thrombocytosis and elevations in one ormore of the hepatic enzymes, ALT (SGPT), AST (SGOT), LDH, GGT and alkaline phosphatase.

OVERDOSAGE
Overdosage can lead to neurological sequelae including encephalopathy, convulsions and coma. Serum levels of ceftazidime can be reduced by haemodialysis or peritoneal dialysis.

PHARMACEUTICAL PRECAUTIONS
positive pressure is produced on constitution due to the release of carbon dioxide. See Administration section for recommended techniques of constitution.

Solutions of ceftazidime in Water for Injections or compatible fluids retain satisfactory potency for 18 hours at a temperature below 30°C, or 7 days in a refrigerator.
Compatibility: Ceftaiidime is compatible with most comrrionly used intravenous fluids. Ceftazidime is less stable in Sodium bicarbonate injection then in other intravenous fluids. It is not recommended as a diluent. Ceftazidime and aminoglycosides should not be mixed in the same giving set or syringe. Precipitation has been reported when vancomycin has been added to ceftazidirne in solution.'Therefore, it would be prudent to flush giving sets and intravenous lines between administration Of these two agents.
Solutions range from light yellow to amber depending on concentration, diluent and storage conditions used. Within the stated recommendations, product potency is not adversely affected by such colour variations.
Ceftazidime at concenjrations between 1 mg/m1 and 40mg/m1 is compatible with;
- 0.9% Sodium Chloride Injection.
- M/6 Sodium Lactate Injection
- Compound Sodium Lactate Injection (Hartmann's Solution)
- 5% Dextrose Injection .
- 0.225% Sodium Chloride and 5% Dextrose Injection
- 0.45% Sodium Chloride and 50% Dextrose Injection
- 0.9% Sodium Chloride and 5% Dextrose Injection
- 0.18% Sodium Chloride and 4% Dextrose Injection
- . 10%6 Dextrose Injection
- Dextran 40 Injection 10% in 0.9% Sodium Chloride Injection
- Dextran 40 Injection 10%6 in 5% Dextrose Injection
- Dextran 70 Injection 6% in 0.9% Sodium Chloride Injection
- Dextran 70 Injection 6% in 5% Dextrose Injection

Ceftazsdime at concentrations between 0.05mg/m1 and 0.25mg/m1 is compatible with Intraperitoneal Dialysis Fluid (Lactate).
Ceftazidime may be constituted for intramuscular use with 0.5% or 1% Lignocaine Hydrochloride Injection.
Both components retain satisfactory potency when ceftazidime at 4mg/m1 is admixed with:
- Hydrocortisone (hydrocortisone sodium phosphate) 1 mg/ml in 0.9% Sodium Chloride injection or 5% Dextrose Injection.
- Cefuroxime (cefuroxime sodium) 3mg/m1 in 0.9% Sodium Chloride Injection.
- Cloxacillin cloxacillin sodium 4mg/m1 in 0.9% Sodium Chloride Injection.
- Heparin 101U/rill or 50 IU/m1 in 0.9% Sodium Chloride Injection.
- Potassium Chloride 10mEq/1 or 40mEq/1 in 0.9% Sodium Chloride Injection.

The contents of a 500mg vial of Ceftazidime for Injection, constituted with 1.5ml Water for . Injections, may be added to metronidazole injection (500mg in 100m1) and both retain their activity.

STORAGE
Store belpw 30°C. Protect from light and moisture.

Keep all medicines out of the reach of children.

PRESENTATION
EvoZid 250 mg: 1 vial of 250 mg dry powder, with 1 ampoule of 5 ml water for injection.

EvoZid 500 mg: 1 vial of 500 mg dry powder, with 1 ampoule of 5 ml water for injection.

EvoZid 1 g: 1 vial of 1 g dry powder, with 1 ampoule of 10 ml water for injection.

ہدایات:۔

صرف آئی وی/ آئی ایم انجکشن کے لئے استعمال کریں۔
استعمال کی مزید تفصیل کے لئے ڈبے کے اندر مہیا کئے گئے پرچے کو دیکھیں۔
دوا کو روشنی اور نمی سے محفوظ ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
ڈاکٹر کی ہدایات کے مطابق استعمال کریں۔
تمام دوائیں بچوں کی پہنچ سے دور رکھیں
صرف رجسٹرڈ ڈاکٹر کے نسخے پر ہی فروخت کی جائے۔