Bosch For Medical Professional Only

Fortazim Injection

(C e f t a z i d i m e)

Sterile Powder for Injection

فورٹازِم انجکشن

(سیفٹازیڈائم)

DESCRIPTION:
Ceftazidime is a semisynthetic, broad-spectrum, beta-lactam antibacterial drug for parenteral administration. It is the pentahydrate of pyridinium, 1-[[7-[[(2-amino-4-thiazolyl)[(1-carboxy1-methylethoxy)imino]acetyl]amino]-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]-, hydroxide, inner salt, [6R-[6α,7β(Z)]]. The molecular formula is $C_{22}H_{32}N_6O_{12}S_2 \cdot 5H_2O$, representing a molecular weight of 636.65.
FORTAZIM is a sterile, dry powdered, mixture of ceftazidime pentahydrate and sodium carbonate. Solution of Fortazim range in color from light yellow to amber, depending on the diluent and volume used.

COMPOSITION:
Each Fortazim 0.25g vial contains:
Ceftazidime U.S.P. ....250 mg
(as pentahydrate)
(Product Specs.: U.S.P.)

Each Fortazim 0.5g vial contains:
Ceftazidime U.S.P. ....500 mg
(as pentahydrate)
(Product Specs.: U.S.P.)

Each Fortazim 1g vial contains:
Ceftazidime U.S.P. ....1000 mg
(as pentahydrate)
(Product Specs.: U.S.P.)

CLINICAL PHARMACOLOGY:
Pharmacodynamics properties:
Pharmacotherapeutic group: Anti-bacterial for systemic use.
Third-generation cephalosporin ATC code: J01DD02

Mechanism of action:
Ceftazidime is a bactericidal agent that acts by inhibition of bacterial cell wall synthesis. Ceftazidime has activity in the presence of some beta-lactamases, both penicillinases and cephalosporinases, of Gram-negative and Gram-positive bacteria.

Microbiology:
Gram-positive bacteria:
- Staphylococcus aureus
- Streptococcus pneumoniae
- Streptococcus pyogenes
- Streptococcus agalactiae
- Staphylococcus epidermidis

Gram-negative bacteria:
- Citrobacter species
- Enterobacter species
- Escherichia coli
- Klebsiella species
- Haemophilus influenzae
- Neisseria meningitidis
- Proteus mirabilis
- Proteus vulgaris
- Pseudomonas aeruginosa
- Serratia species
- Acinetobacter species
- Citrobacter diversus
- Citrobacter freundii
- Salmonella species
- Shigella species
- Haemophilus parainfluenzae
- Morganella morganii
- Neisseria gonorrhoeae
- Yersinia enterocolitica

Anaerobic bacteria:
- Bacteroides species
- Clostridium species (Not including Clostridium difficile)
- Peptostreptococcus species

Pharmacokinetic properties
Absorption:
After intramuscular administration of 500 mg and 1 g of ceftazidime, peak plasma levels of 18 and 37 mg/l respectively are achieved rapidly. Five minutes after intravenous bolus injection of 500 mg, 1 g or 2 g, plasma levels are 46, 87 and 170mg/l, respectively.

Distribution:
The serum protein binding of ceftazidime is low at about 10%.Concentrations in excess of the MIC for common pathogens can be 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. Concentration of 4 to 20 mg/l or more are achieved in the CSF when the meninges are inflamed.

Biotransformation
Ceftazidime is not metabolised.

Elimination:
After parenteral administration plasma levels decrease with a half-life of about 2 h. Ceftazidime is excreted unchanged into the urine by glomerular filtration; approximately 80 to 90 % of the dose is recovered in the urine within 24 h. Less than 1 % is excreted via the bile.

Specific Populations
Renal impairment
Elimination of ceftazidime is decreased in patients with impaired renal function and the dose should be reduced

Hepatic impairment
The presence of mild to moderate hepatic dysfunction had no effect on the pharmacokinetics of ceftazidime.

Pediatrics:
The half-life of ceftazidime is prolonged in preterm and term neonates by 4.5 to 7.5 hours after doses of 25 to 30 mg/kg. However, by the age of 2 months the half-life is within the range for adults.

Elderly:
The reduced clearance observed in elderly patients was primarily due to age-related decrease in renal clearance of ceftazidime. The mean elimination half-life ranged from 3.5 to 4 hours following single or 7 days repeat BID dosing of 2 g IV bolus injections in elderly patients 80 years or older.

THERAPEUTIC INDICATIONS:
- Lower Respiratory Tract Infections including pneumonia
- Skin and Skin-Structure Infections
- Urinary Tract Infections

- Bacterial Septicemia
- Bone and Joint Infections
- Gynecologic Infections
- Intra-abdominal Infections, including peritonitis
- Central Nervous System Infections, including meningitis

DOSAGE AND ADMINISTRATION:

Adults

The usual adult dosage is 1 gram administered intravenously or intramuscularly every 8 to 12 hours.

Adult	Dose	Frequency
Usual recommended dosage	1 gram intravenous or intramuscular	every 8 to 12 hours
Uncomplicated urinary tract infection	250 mg intravenous or intramuscular	every 12 hours
Bone and joint infections	2 grams intravenous	every 12 hours
Complicated urinary tract infections	500 mg intravenous or intramuscular	every 8 to 12 hours
Uncomplicated pneumonia; mild skin and skin-structure infections	500 mg to 1 gram intravenous or intramuscular	every 8 hours
Serious gynecological and intra-abdominal infections	2 grams intravenous	every 8 hours
Meningitis	2 grams intravenous	every 8 hours
Very severe life-threatening infections, especially in immunocompromised Patients	2 grams intravenous	every 8 hours
Lung infections in patients with cystic fibrosis with normal renal function	30 to 50 mg/kg intravenous to a maximum of 6 grams per day	every 8 hours

Neonates, Infants and children:

Neonates (0-4 weeks)	30 mg/kg intravenous	every 12 hours
Infants and children (1 month – 12 years)	30 to 50 mg/kg intravenous to a maximum of 6 grams per day	every 8 hours

Elderly:

The daily dose should not normally exceed 3 g in those over 80 years of age.

Patients with renal impairment:

Ceftazidime is excreted by the kidneys, almost exclusively by glomerular filtration. Therefore, in patients with impaired renal function (glomerular filtration rate [GFR]] <50 mL/min), it is recommended that the dosage of ceftazidime be reduced to compensate for its slower excretion.

Recommended Maintenance Dosages of FORTAZIM in Renal Impairment

Creatinine Clearance (mL/min)	Recommended Unit Dose of FORTAZIM	Frequency of Dosing
50-31	1 gram	every 12 hours
30-16	1 gram	every 24 hours
15-6	500 mg	every 24 hours
less than 5	500 mg	every 48 hours

If the dose recommended in previous table is lower than that recommended for patients with renal impairment, the lower dose should be used.

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

In patients undergoing hemodialysis, a loading dose of 1 gram is recommended, followed by 1 gram after each hemodialysis period.

FORTAZIM can also be used in patients undergoing intraperitoneal dialysis and continuous ambulatory peritoneal dialysis. In such patients, a loading dose of 1 gram of FORTAZIM may be given, followed by 500 mg every 24 hours. In addition to IV use, FORTAZIM can be incorporated in the dialysis fluid at a concentration of 250 mg for 2L of dialysis fluid.

Method of administration:

INTRAMUSCULAR ADMINISTRATION:

For IM administration, FORTAZIM should be constituted with Sterile Water for Injection, or Bacteriostatic Water for Injection, or 0.5% or 1% Lidocaine Hydrochloride Injection.

INTRAVENOUS ADMINISTRATION :

For direct intermittent IV administration:

Constitute FORTAZIM with Sterile Water for Injection. Slowly inject directly into the vein over a period of 3 to 5 minutes or give through the tubing of an administration set while the patient is also receiving one of the compatible IV fluids.

For IV infusion:

Constitute the 250-mg, 500-mg or 1-gram, vial and add an appropriate quantity of the resulting solution to an IV container with one of the compatible IV fluids.

Reconstitution

Size	Amount of Diluent to be Added (mL)
Intramuscular	
250-mg vial	1
500-mg vial	1.5
1-gram vial	3
Intravenous	
250-mg vial	2.5
500-mg vial	5.3
1-gram vial	10

CONTRAINDICATIONS:

Hypersensitivity to ceftazidime, to any other cephalosporin or to excipient or 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

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.

Spectrum of activity

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. Ceftazidime is susceptible to hydrolysis by several of the extended spectrum beta lactamases (ESBLs).

Pseudomembranous colitis

Antibacterial agent-associated colitis and pseudo-membranous colitis have been reported with nearly all anti-bacterial agents, including ceftazidime, and may range in severity from mild to life-threatening. Medicinal products that inhibit peristalsis should not be given.

Renal function

Concurrent treatment with high doses of cephalosporins and nephrotoxic medicinal products such as aminoglycosides or potent diuretics (e.g. furosemide) may adversely affect renal function. Patients with renal impairment should be closely monitored for both safety and efficacy.

Overgrowth of non-susceptible organisms

Prolonged use may result in the overgrowth of non-susceptible organisms (e.g. Enterococci, fungi).

Test and assay interactions

Ceftazidime does not interfere with enzyme-based tests for glycosuria, but slight interference (false-positive) may occur with copper reduction methods (Benedict's, Fehling's, Clinitest).

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.

DRUG INTERACTIONS:
Concurrent use of high doses with nephrotoxic medicinal products may adversely affect renal function.
Chloramphenicol is antagonistic in vitro with ceftazidime and other cephalosporins.

ADVERSE EFFECTS:
Common:
Eosinophilia, Thrombocytosis, Phlebitis or thrombophlebitis with intravenous administration, Diarrhoea Transient elevations in one or more hepatic enzymes, Maculopapular or urticarial rash, Pain and/or inflammation after intramuscular injection.

Uncommon:
Candidiasis (including vaginitis and oral thrush), Neutropenia, Leucopenia, Thrombocytopenia, Headache, Dizziness, Antibacterial agent-associated diarrhea and colitis, Abdominal pain, Nausea, Vomiting, Pruritus, Transient elevations of blood urea, blood urea nitrogen and/or serum creatinine, Fever.

Very rare:
Interstitial nephritis, acute renal failure

Not Known:
Agranulocytosis, Haemolytic anaemia, Lymphocytosis, Anaphylaxis (including bronchospasm and/or hypotension), Neurological sequelae, Paraesthesia, Bad taste, Jaundice, Toxic epidermal necrolysis, Stevens-Johnson syndrome, Erythema multiforme, Angioedema, Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)

USE IN PREGNANCY AND LACTATION:
Pregnancy:
Pregnancy Category B
No adequate and well-controlled studies in pregnant women. This drug should be used during pregnancy only if clearly needed.

Lactation:
Ceftazidime is excreted in human milk in low concentrations. Caution should be exercised when FORTAZIM is administered to a nursing woman.

OVERDOSE:
Ceftazidime overdosage has occurred in patients with renal failure. Reactions have included seizure activity, encephalopathy, asterixis, neuromuscular excitability, and coma. Hemodialysis or peritoneal dialysis may aid in the removal of ceftazidime from the body.

Incompatibilities:
Fortazim is less stable in Sodium Bicarbonate Injection than in other intravenous fluids. It is not recommended as a diluent. Fortazim and aminoglycosides should not be mixed in the same giving set or syringe. Precipitation has been reported with vancomycin added to ceftazidime in solution.

Special precautions for disposal and other handling:
All sizes of vials of Fortazim 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.

Shelf life
Fortazim Injection has a shelf life of 3 years.

STABILITY:
Reconstituted vials of Fortazim with water for injection or compatible fluids retain satisfactory potency for 18 hours at room temperature or 7 days in a refrigerator.

PRESENTATION:
Fortazim 0.25g Injection: Pack of 1 vial+1 Ampoule of 3ml sterile water for injection.
Fortazim 0.5g Injection: Pack of 1 vial+1 Ampoule of 5ml sterile water for injection.
Fortazim 1g Injection: Pack of 1 vial+1 Ampoule of 10ml sterile water for injection.

Storage and Instruction:
For Intramuscular/Intravenous use.
Effervescence occurs on addition of water for injection.
Protect from heat, sunlight & moisture, store below 25°C.
The expiration date refer to the product correctly stored at the required condition.
Keep out of the reach of children.
Patients and healthcare professionals can also report suspected adverse drug reaction at ade@bosch-pharma.com
To be sold on prescription of a registered medical practitioner only.

پٹھوں/وریدی استعمال کے لئے۔

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

ہدایات:۔ دھوپ، گرمی اور نمی سے محفوظ ۲۵ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
بچوں کی پہنچ سے دُور رکھیں۔ صرف مستند ڈاکٹر کے نسخے پر فروخت کے لئے۔

Manufactured by:
Bosch Pharmaceuticals (Pvt) Ltd.
221-223, Sector 23, Korangi Industrial Area,
Karachi - Pakistan

ISO 9001:2015 Certified Company

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(Ceftazidime)

Sterile Powder for Injection

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(سیفٹازیڈائم)

RENAISSANCE INSPECTION & CERTIFICATION AGENCY

حلال

HALAAL

Bosch