Ceftazim AV 2.5 g

Ceftazidime 2 g & Avibactam 0.5 g

IV Injection for infusion

Composition:
Ceftazim AV 2.5 g IV Injection for Infusion: Each vial contains Ceftazidime Pentahydrate USP equivalent to Ceftazidime 2 g and Avibactam Sodium INN equivalent to Avibactam 0.5 g.

Description:
Ceftazim AV is an antibacterial combination product consisting of the semisynthetic cephalosporin ceftazidime pentahydrate and the beta-lactamase inhibitor avibactam sodium for intravenous administration.

Pharmacology:
The ceftazidime component of **Ceftazim AV** is a broad-spectrum cephalosporin antibiotic with in vitro activity against certain gram-negative and gram-positive bacteria. The bactericidal action of ceftazidime is mediated through binding to essential penicillin-binding proteins (PBPs). The avibactam component of **Ceftazim AV** is a beta-lactamase inhibitor that inactivates certain beta-lactamases that degrade ceftazidime. Avibactam does not decrease the activity of ceftazidime against ceftazidime-susceptible organisms.

Indications:
Ceftazim AV is indicated in adults and pediatric patients aged 3 months and older for the treatment of the following infections:
- Complicated intra-abdominal infections (cIAI)
- Complicated urinary tract infections (cUTI), including pyelonephritis
- Hospital-acquired bacterial pneumonia (HABP), including ventilator-associated bacterial pneumonia (VABP)

Dosage & Administration:

Dosage in adults with creatinine clearance (CrCL) > 50 mL/min

Type of infection	Dose	Frequency	Infusion time	Duration of treatment
Complicated intra-abdominal infections (cIAI)	2.5 grams	Every 8 hours	2 hours	5 to 14 days
Complicated urinary tract infections (cUTI), including pyelonephritis				7 to 14 days
Hospital-acquired bacterial pneumonia (HABP), including ventilator-associated bacterial pneumonia (VABP)				7 to 14 days

Dosage adjustments in adult patients with renal impairment

Estimated Creatinine Clearance (mL/minute)[a]	Dose[b]	Frequency
31 to 50	**Ceftazim AV** 1.25 grams (ceftazidime 1 gram and avibactam 0.25 grams) intravenously	Every 8 hours
16 to 30	**Ceftazim AV** 0.94 grams (ceftazidime 0.75 grams and avibactam 0.19 grams) intravenously	Every 12 hours
6 to 15[c]	**Ceftazim AV** 0.94 grams (ceftazidime 0.75 grams and avibactam 0.19 grams) intravenously	Every 24 hours
≤ 5[c]	**Ceftazim AV** 0.94 grams (ceftazidime 0.75 grams and avibactam 0.19 grams) intravenously	Every 48 hours

a - As calculated using the Cockcroft-Gault formula.
b - All doses of **Ceftazim AV** are administered over 2 hours.
c - Both ceftazidime and avibactam are hemodialyzable; thus, administer **Ceftazim AV** after hemodialysis on hemodialysis days.

Dosage in pediatric patients

Type of Infection	Age Range	Dose	Frequency	Infusion Time	Duration of Treatment
Complicated intra-abdominal infections (cIAI)* Complicated urinary tract infections (cUTI), including pyelonephritis	2 years to less than 18 years	**Ceftazim AV** 62.5 mg/kg to a maximum of 2.5 grams (Ceftazidime 50 mg/kg and avibactam 12.5 mg/kg to a maximum dose of ceftazidime 2 grams and avibactam 0.5 grams)	Every 8 hours	2 hours	cIAI: 5 to 14 days cUTI: 7 to 14 days
	6 months to less than 2 years	**Ceftazim AV** 62.5 mg/kg (Ceftazidime 50 mg/kg and avibactam 12.5 mg/kg)			
	3 months to less than 6 months	**Ceftazim AV** 50 mg/kg (Ceftazidime 40 mg/kg and avibactam 10 mg/kg			

*For treatment of cIAI, metronidazole should be given concurrently.

Dosage adjustments in pediatric patients with renal impairment

Estimated eGFR (mL/min/1.73m2)[a]	Dose[b]	Frequency
31 to 50	**Ceftazim AV** 31.25 mg/kg to a maximum of 1.25 grams (ceftazidime 25 mg/kg and avibactam 6.25 mg/kg to a maximum dose of ceftazidime 1 gram and avibactam 0.25 grams)	Every 8 hours
16 to 30	**Ceftazim AV** 23.75 mg/kg to a maximum of 0.94 grams (ceftazidime 19 mg/kg and avibactam 4.75 mg/kg to a maximum dose of ceftazidime 0.75 grams and avibactam 0.19 grams)	Every 12 hours
6 to 15	**Ceftazim AV** 23.75 mg/kg to a maximum of 0.94 grams (ceftazidime 19 mg/kg and avibactam 4.75 mg/kg to a maximum dose of ceftazidime 0.75 grams and avibactam 0.19 grams)	Every 24 hours
≤ 5[c]	**Ceftazim AV** 23.75 mg/kg to a maximum of 0.94 grams (ceftazidime 19 mg/kg and avibactam 4.75 mg/kg to a maximum dose of ceftazidime 0.75 grams and avibactam 0.19 grams)	Every 48 hours

a - As calculated using the Schwartz bedside formula.
b - All doses of **Ceftazim AV** are administered over 2 hours.
c - Both ceftazidime and avibactam are hemodialyzable; thus, administer **Ceftazim AV** after hemodialysis on hemodialysis days.

Method of Administration:
Ceftazim AV is supplied as a dry powder, which must be constituted and subsequently diluted, using aseptic technique prior to intravenous infusion.

Reconstitution Direction:
(a) Constitute the powder in the **Ceftazim AV** vial with 10 mL of one of the following solutions:
- Sterile water for injection, USP
- 0.9% of sodium chloride injection, USP (normal saline)
- 5% of dextrose injection, USP
- All combinations of dextrose injection and sodium chloride injection, USP, containing up to 2.5% dextrose, USP, and 0.45% sodium chloride, USP, or
- Lactated Ringer's injection, USP

(b) Mix gently and ensure that the contents are dissolved completely. The constituted **Ceftazim AV** solution will have an approximate ceftazidime concentration of 167 mg/mL and an approximate avibactam concentration of 42 mg/mL. The final volume is approximately 12 mL. The constituted solution is not for direct injection. The constituted solution must be diluted before intravenous infusion.

(c) Prepare the required dose for intravenous infusion by withdrawing the appropriate volume determined from the following table from the constituted vial.

Preparation of Ceftazim AV doses for Adult and Pediatric Patients (Weighing 40 kg or More)	
Ceftazim AV Dose	Volume to Withdraw from Constituted Vial for Further Dilution to 50 to 250[a] mL
2.5 grams (2 grams and 0.5 grams)	12 mL (entire contents)
1.25 grams (1 gram and 0.25 grams)	6 mL
0.94 grams (0.75 grams and 0.19 grams)	4.5 mL
[a.] Dilution to 250 mL should only be used for the 2.5 grams dose	

(d) Before infusion, dilute the withdrawn volume of the constituted **Ceftazim AV** solution further with the same diluent used for constitution of the powder (except sterile water for injection), to achieve a ceftazidime concentration of 8 to 40 mg/mL and an avibactam concentration of 2 to 10 mg/mL in an infusion bag. If sterile water for injection was used for constitution, use any of the other appropriate constitution diluents for dilution.

(e) Mix gently and ensure that the contents are dissolved completely. Visually inspect the diluted **Ceftazim AV** solution (for administration) for particulate matter and discoloration prior to administration (the color of the **Ceftazim AV** infusion solution for administration ranges from clear to light yellow).

(f) Upon constitution with appropriate diluent, the constituted **Ceftazim AV** solution may be held for no longer than 30 minutes prior to transfer and dilution in a suitable infusion bag. Use the diluted **Ceftazim AV** solution in the infusion bags within 12 hours when stored at room temperature.

(g) The diluted **Ceftazim AV** solution in the infusion bags may be stored under refrigeration at 2 to 8°C up to 24 hours following dilution and used within 12 hours of subsequent storage at room temperature.

Overdose:
In the event of overdose, discontinue **Ceftazim AV** and institute general supportive treatment. Ceftazidime and avibactam can be removed by hemodialysis.

Contraindications:
Ceftazim AV is contraindicated in patients with known serious hypersensitivity to the components of **Ceftazim AV** (ceftazidime and avibactam), avibactam-containing products or other members of the cephalosporin class.

Warnings & Precautions:
Decreased efficacy in adult cIAI patients with baseline CrCl of 30 to less than or equal to 50 mL/ min: Monitor CrCl at least daily in adult and pediatric patients with changing renal function and adjust dose of **Ceftazim AV** accordingly.

Hypersensitivity reactions: Includes anaphylaxis and serious skin reactions. Cross-hypersensitivity may occur in patients with a history of penicillin allergy. If an allergic reaction occurs, discontinue **Ceftazim AV**.

Clostridium difficile-associated diarrhea (CDAD): CDAD has been reported with nearly all systemic antibacterial agents, including **Ceftazim AV**. Evaluate if diarrhea occurs.

Central Nervous System Reactions: Seizures and other neurologic events may occur, especially in patients with renal impairment. Adjust dose in patients with renal impairment.

Side effects:
Adult cIAI, cUTI and HABP/VABP Patients: The most common adverse reactions in cIAI (≥ 5%, when used with metronidazole) patients are diarrhea, nausea and vomiting. The most common adverse reactions (3%) in cUTI patients are diarrhea and nausea. The most common adverse reactions (≥ 5%) in HABP/VABP patients were diarrhea and vomiting.

Pediatric cIAI and cUTI Patients: The most common adverse reactions (≥ 3%) in pediatric patients were vomiting, diarrhea, rash, and infusion site phlebitis.

Drug interactions:
Clinical interaction study of **Ceftazim AV** or avibactam alone with probenecid has not been conducted, co-administration of **Ceftazim AV** with probenecid is not recommended.

Use in Special Population:
Pregnancy: There are no adequate and well-controlled studies of **Ceftazim AV**, ceftazidime, or avibactam in pregnant women.

Lactation: No information is available on the effects of ceftazidime and avibactam on the breast-fed child or on milk production.

Storage
Store below 25°C, keep in dry place & protect from light. Keep out of the reach of children.

Packing
Ceftazim AV 2.5 g IV Injection for Infusion: Each box contains 1 vial of 2.5 grams (ceftazidime 2 grams and avibactam 0.5 grams) with 1 ampoule of 10 mL sterile water for injection.

Manufactured by:
ARISTOPHARMA LTD.
GAZIPUR, BANGLADESH

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