Zetaro™

Ceftaroline Fosamil

2493

Presentation
Zetaro™ IV infusion: Each vial contains Ceftaroline Fosamil for Injection INN eqv. to Ceftaroline Fosamil 600 mg.

Pharmacology
Ceftaroline is a cephalosporin antibacterial drug with activity against Gram positive and Gram negative bacteria. Ceftaroline shows bactericidal activity due to inhibition of bacterial cell wall synthesis by binding to penicillin binding proteins (PBPs). Ceftaroline is also active against Methicillin-resistant *Staphylococcus aureus* and Penicillin-resistant *Streptococcus pneumoniae* due to its affinity for the altered PBPs found in these organisms.

Indications
• **Acute Bacterial Skin and Skin Structure Infections (ABSSSI)** caused by susceptible isolates of the following Gram positive and Gram negative microorganisms- *Staphylococcus aureus* (including methicillin-susceptible and resistant isolates), *Streptococcus pyogenes, Streptococcus agalactiae, Escherichia coli, Klebsiella pneumoniae* and *Klebsiella oxytoca.*

• **Community-Acquired Bacterial Pneumonia (CABP)** caused by susceptible isolates of the following Gram positive and Gram negative microorganisms- *Streptococcus pneumoniae* (including cases with concurrent bacteremia), *Staphylococcus aureus*, *Haemophilus influenzae, Klebsiella pneumoniae, Klebsiella oxytoca* and *Escherichia coli.*

Dosage and administration
The duration of therapy should be guided by the severity and site of infection and the patient's clinical and bacteriological progress.

Indications	Age Range	Dosage	Infusion Time	Duration
Acute Bacterial Skin and Skin Structure Infections	18 years and older	600 mg every 12 hours	5 to 60 minutes	5 to 14 days
	≥2 years to <18 years (>33 kg)	600 mg every 12 hours	5 to 60 minutes	5 to 14 days
	≥2 years to <18 years (≤33kg)	12 mg/kg every 8 hours	5 to 60 minutes	5 to 14 days
	2 months to <2 years	8 mg/kg every 8 hours	5 to 60 minutes	5 to 14 days
	0* to <2 months *At leat 34 weeks gestational age and 12 days postnatal age	6 mg/kg every 8 hours	30 to 60 minutes	5 to 14 days
Community -Acquired Bacterial Pneumonia	18 years and older	600 mg every 12 hours	5 to 60 minutes	5 to 7 days
	≥2 years to <18 years (>33 kg)	600 mg every 12 hours	5 to 60 minutes	5 to 14 days
	≥2 years to <18 years (≤33kg)	12 mg/kg every 8 hours	5 to 60 minutes	5 to 14 days
	2 months to <2 years	8 mg/kg every 8 hours	5 to 60 minutes	5 to 14 days

Dosage Adjustments in Patients with Renal Impairment

Adult Patients:

Estimated $CrCl_a$ (ml/min)	Recommended Dosage Regimen for Ceftaroline
>50	No dosage adjustment necessary
>30 to ≤50	400 mg IV (over 5 to 60 minutes) every 12 hours
≥15 to ≤30	300 mg IV (over 5 to 60 minutes) every 12 hours
End-stage renal disease, including hemodialysis$_b$	200 mg IV (over 5 to 60 minutes) every 12 hours$_c$

a Creatinine clearance (CrCl) estimated using the Cock Croft-Gault formula.

b End-stage renal disease is defined as CrCl <15 ml/min.

c Ceftaroline is hemodialyzable; thus, Ceftaroline should be administered after hemodialysis on hemodialysis days.

Pediatrics:
No dosage adjustment is required in pediatric patients with CrCL >50 ml/min/1.73 m^2, estimated using the Schwartz equation. There is insufficient information to recommend a dosage regimen for pediatric patients with CrCL <50 ml/min/1.73 m^2.

Preparation of the solution for intravenous infusion & method of administration
Aseptic technique must be followed in preparing the infusion solution.

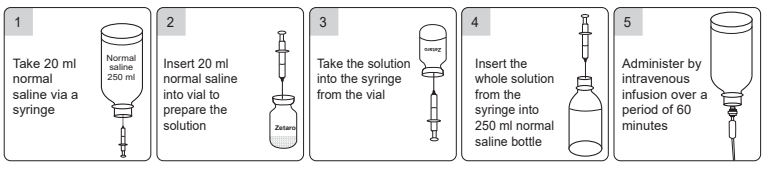
Reconstitution: The contents of the vial should be reconstituted with 20 ml 0.9% Sodium chloride solution (normal saline). Mix gently to constitute and check to see that the contents have dissolved completely.

Dilution: The reconstituted solution must be further diluted with normal saline to achieve a volume of 50 ml, 100 ml or 250 ml before intravenous infusion into patients.

Administration: The resulting diluted solution should be administered according to the dose selected over 5 to 60 minutes for standard dose in infusion volumes of 50 ml, 100 ml or 250 ml.

Infusion volumes for paediatric patients will vary according to the weight of the child. The concentration of Ceftaroline fosamil in infusion solution for administration should not exceed 12 mg/ml.

Reconstitution and dilution process of Ceftaroline fosamil 600 mg with 250 ml 0.9% Sodium chloride solution (normal saline):



Contraindications
Ceftaroline is contraindicated in patients with known serious hypersensitivity to Ceftaroline or other members of the cephalosporin class. Anaphylaxis has been reported with Ceftaroline.

Warning and precaution
Serious hypersensitivity (anaphylactic) reactions have been reported with beta-lactam antibacterial drugs, including Ceftaroline. If a hypersensitivity reaction occurs, discontinue Ceftaroline. *Clostridium difficile*-associated diarrhea (CDAD) has been reported with nearly all systemic antibacterial agents, including Ceftaroline. Evaluate if diarrhea occurs.

Neurological adverse reactions have been reported in patients treated with cephalosporins, including Ceftaroline. If neurological adverse reactions occur, consider discontinuing Ceftaroline or making appropriate dosage adjustments in patients with renal impairment.

If anemia develops during or after therapy, a diagnostic workup for drug-induced hemolytic anemia should be performed and consideration given to discontinuation of Ceftaroline.

Side effects
The common side effects include diarrhea, nausea, vomiting, abdominal pain, headache, dizziness, rash, pruritus, increased transaminases, phlebitis, pyrexia and infusion site reactions (erythema, phlebitis, pain). The uncommon side effects are anemia, leucopenia, thrombocytopenia, hypersensitivity/anaphylaxis, urticaria, *Clostridium difficile* colitis, prolonged prothrombin time, increased blood creatinine; and rarely eosinophilia.

Use in Pregnancy & Lactation
No clinical data on pregnancy is available for Ceftaroline. Animal studies with Ceftaroline fosamil do not indicate harmful effects with respect to fertility, pregnancy, parturition or postnatal development. Ceftaroline should not be used during pregnancy unless clearly necessary and only if the potential benefit outweighs the possible risk.

It is not known whether Ceftaroline is excreted in human milk, but because many beta-lactams are excreted in breast milk, women who are breast-feeding should be treated with Ceftaroline only if clearly indicated. Interruption of breast-feeding is recommended.

Use in pediatric patients
Safety and effectiveness of Ceftaroline in pediatric patients less than 34 weeks gestational age and less than 12 days postnatal age for the treatment of ABSSSI have not been established. Safety and effectiveness of Ceftaroline in pediatric patients below the age of 2 months for the treatment of CABP have not been established as no data are available.

Renal Impairment
Dosage adjustment is required in adult patients with moderate (CrCl >30 to ≤50 ml/min) or severe (CrCl ≥ 15 to ≤30 ml/min) renal impairment and in patients with end-stage renal disease (ESRD – defined as CrCl <15 ml/min), including patients on hemodialysis (HD). There is insufficient information to recommend a dosage regimen for pediatric patients with CrCl <50 ml/min.

Hepatic Insufficiency
The pharmacokinetics of Ceftaroline in patients with hepatic impairment have not been established. As Ceftaroline does not appear to undergo significant hepatic metabolism, the systemic clearance of Ceftaroline is not expected to be significantly affected by hepatic impairment.

Drug interactions
No clinical drug-drug interaction studies have been conducted with Ceftaroline. There is minimal potential for drug-drug interactions between Ceftaroline and CYP450 substrates, inhibitors, or inducers; drugs known to undergo active renal secretion; and drugs that may alter renal blood flow.

Overdose
Ceftaroline overdosage has occurred in patients with renal impairment. Reactions have included neurological sequelae, including encephalopathy. In the event of overdose, Ceftaroline should be discontinued and general supportive treatment given.

Storage
Prior to reconstitution, do not store Ceftaroline Fosamil powder for infusion above 30°C and should be used immediately after reconstitution. The diluted solution in the infusion bottle should be used within 6 hours when stored at room temperature or within 24 hours when stored under refrigeration at 2° to 8° C. Keep away from light and out of the reach of children.

Commercial Pack
Zetaro™ IV infusion: Each box contains 1 vial of Ceftaroline Fosamil 600 mg, 1 glass bottle of 250 ml normal saline, one 20 ml disposable syringe, 1 infusion set with butterfly needle, 1 first aid band, 1 alcohol pad & 1 hanger.

Manufactured by
Incepta Pharmaceuticals Ltd
Savar, Dhaka, Bangladesh
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