New drugs

Ceftaroline fosamil

Approved indication: complicated skin and soft tissue infections, community-acquired pneumonia

Zinforo (AstraZeneca)
vials containing 600 mg powder for infusion

Australian Medicines Handbook section 5.1.3

Ceftaroline fosamil is a cephalosporin with broad-spectrum in vitro activity against Gram-positive bacteria, including Staphylococcus aureus, Streptococcus pyogenes and S. pneumoniae, and some Gram-negative bacteria, including Escherichia coli, Haemophilus influenzae and Klebsiella pneumoniae. It is also effective against methicillin-resistant S. aureus (MRSA) and penicillin non-susceptible S. pneumoniae because it binds to the altered penicillin-binding proteins produced by these bacteria.

Ceftaroline fosamil is a prodrug which is converted into active ceftaroline by phosphatases in the plasma. Following a single intravenous dose of 600 mg, almost 90% is excreted by the kidneys with a mean terminal half-life of 2.5 hours. Dose adjustment is required in patients with moderate renal impairment (creatinine clearance >30–50 mL/minute) and it is not recommended in severe renal impairment or end-stage renal disease. Pharmacokinetic drug interactions are not expected as ceftaroline does not inhibit or induce P450 cytochromes and is not metabolised by these enzymes.

The approval of ceftaroline for complicated skin and soft tissue infections is based on two similarly designed phase III randomised controlled trials – CANVAS 1 and 2. A total of 1378 patients requiring intravenous antibiotics received ceftaroline 600 mg every 12 hours or ceftriaxone 1 g every 24 hours for 5–7 days. In total, 1228 hospitalised patients requiring intravenous antibiotics (but not in the intensive care unit) received ceftaroline 600 mg and was withdrawn. One patient receiving ceftaroline were withdrawn. One patient had Clostridium difficile-associated diarrhoea and the others had allergic reactions. There were three deaths in the ceftaroline group – causes included respiratory failure, neck cancer and cardiopulmonary insufficiency.

The most common treatment-emergent adverse events in the skin trials were nausea (5.9%), headache (5.2%), diarrhoea (4.9%), pruritus (3.5%), rash (3.2%) and vomiting (2.9%). Four patients receiving ceftaroline were withdrawn. One patient had Clostridium difficile-associated diarrhoea and the others had allergic reactions. There were three deaths in the ceftaroline group – causes included respiratory failure, neck cancer and cardiopulmonary insufficiency.

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ceftaroline, as it is with other cephalosporins. Doctors should be aware that patients allergic to penicillins may also be allergic to ceftaroline.

There are no human data for ceftaroline in pregnancy or lactation so it should only be used if the benefits outweigh the potential harms. Interruption of breastfeeding is recommended. The safety and efficacy of ceftaroline in children is currently unknown.

Ceftaroline was non-inferior to comparative treatments in phase III trials and provides another option for hospitalised patients with complicated skin infections or community-acquired pneumonia. It has efficacy against infections caused by MRSA and drug-resistant *S. pneumoniae*, but is less effective against some Gram-negative pathogens. It should only be used for infections that are proven or are strongly suspected to be caused by susceptible bacteria. Antibiotic stewardship is important, particularly as ceftaroline has broad-spectrum activity.

*†* manufacturer provided the product information

**REFERENCES**


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The Transparency score (†) is explained in ‘New drugs: T-score for transparency’, *Aust Prescr* 2011;34:26–7.

* At the time the comment was prepared, information about this drug was available on the website of the Food and Drug Administration in the USA (www.fda.gov).

† At the time the comment was prepared, a scientific discussion about this drug was available on the website of the European Medicines Agency (www.ema.europa.eu).